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TYPHUS FEVER

With special reference to its incidence in India

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HISTORICAL

History shows that typhus fever was for a long time confused with typhoid fever and it was only about a century ago that the difference was made by Gerhard (1837) and Stille (1838). But the disease was known to occur in ancient times and middle ages and it was Fracastorius (1546) who in the earlier part of the sixteenth century gave a clear account of the disease ('febris pestilens') which prevailed in Italy after the great famine of 1508 and 1528. From the sixteenth to the nineteenth century several epidemics occurred in European countries and they were frequently associated with war when famine, general poverty and distress of every kind were present. The disease was prevalent among troops as well as civilian population. Poland and Russia were long recognised as two major endemic centres of typhus fever in Europe. For many years the true etiology and transmission of the disease were unknown. Ricketts (1906) first observed certain organisms in guineapigs and monkeys while experimenting with Rocky mountain spotted fever. Nicolle *et al* (1909) demonstrated that the disease is transmitted by lice. In the year 1916 Rocha-Lima found certain cellular inclusions (Rickettsia bodies) in the intestine of lice fed on human cases of typhus fever. He regarded them as the causative organism of epidemic typhus fever and proposed the name *Rickettsia prowazeki* in honour of the scientists Ricketts and Prowazek both of whom succumbed from typhus fever while studying the disease. In the same year Weil and Felix (1916) introduced the agglutination test with *Bacillus proteus X19* for identifying the disease.

GENERAL DESCRIPTION OF THE DISEASE

Typhus group of fevers occur in many different parts of the world and although they are shown to be caused by a number of species of the genus Rickettsiae, they are linked up together into a common group designated as typhus fever. Even before the etiology of the disease was clarified, typhus fever was all along recognised as a very infectious disease. The agency through which the infection spreads from man to man came to be known later (1909) and the various arthropod vectors were identified to be responsible for the transmission of the disease.

The *incubation* period of typhus fever is taken on an average to be 8 to 14 days. The following are some of the outstanding clinical features practically common to all, but differing only in certain points which help each one of them to be grouped into a separate clinical entity:

Initial Symptoms—Typhus fever is characterised by sudden onset of fever with or without rigor, the temperature rising to 104°F. This is accompanied by malaise, headache, pains all over the body, photophobia and vomiting. The face is flushed, tongue coated, conjunctivae injected and breath often offensive. The pulse rate is comparatively slow and the systolic blood pressure is low. Nervous symptoms develop early and include clouding of consciousness, delirium and other mental excitement followed by drowsiness and stuporous state which form a marked feature of the disease. Enlargement of the spleen is noticeable in some cases. Bowels are generally constipated and there is no abdominal distension. Respiratory symptoms include bronchial catarrh.

Progress—The temperature is continued as a high remittent type and in favourable cases it lasts for a period of 2 to 3 weeks, when it comes down by lysis. The characteristic rash appears from third to seventh day and varies from an erythematous flush to macules or papules with a tendency to become petechial and occasionally haemorrhagic. In addition to rash there is a subcuticular mottling. The mode of appearance of rash, its distribution, and its character vary in different types of typhus fever. The rash when fully developed is distributed all over the body with the exception of face, soles of the feet and palms of the hands in some cases. The rash persists for a period of 10 days and then fades away slowly leaving a brown stain for some days. After defervescence the general weakness, circulatory disturbances and mental symptoms persist for a fortnight and may become worse. Besides cardiac weakness, pneumonia is one of the frequent complications. Mortality rate varies with different types of typhus fever, the highest figure (50 to 100 per cent varying with different epidemics) being recorded with louse typhus (epidemic typhus) and the lowest figure (1 to 4 per cent) with flea typhus (endemic typhus). In tsutsugamushi disease (mite typhus) the death rate was found to be 20 to 30 per cent whereas with that of Rocky mountain spotted fever (tick typhus) 5 to 50 per cent.

Clinical Pathology—Urine is high coloured, albumen may appear and diazo-reaction is often noted. Blood picture does not show anything definite but a moderate leucocytosis has been observed in many cases. Owing to the similarity of the clinical symptoms with enteric group of fever Widal reaction has been worked out and although a group reaction is obtained in low dilution in some cases, it gives invariably a negative result in the end. Wassermann reaction was found to be positive during the febrile period of the disease but became negative when convalescence set in. Occasionally *B. proteus vulgaris* has been isolated from the blood, stool and urine of the patient. The significant finding was that the serum gives agglutination reaction with the strains of *B. proteus.*

Bacteriology—The typhus group of fevers are caused by micro-organisms which are included under the genus Rickettsia. These are small granule-like bodies with a diameter usually less than 0·5 microns. They stain badly with aniline dyes but take a purple colour with Giemsa and are Gram-negative. In their morphology they generally appear as diplococcoid but show marked pleomorphism. They are found inside the tissues of their mammalian host and arthropod vectors. The pathogenic Rickettsiae are always intracellular in position and are found either in the cytoplasm or in the nucleus. Inside the human body the virus circulates in the blood during the febrile period (7th to 12th day of the disease) and is taken up by the respective insect vector. The infective nature of the disease was well recognised and the blood was found to be infective for guineapigs and monkeys. The Rickettsia bodies cannot be isolated from the blood in the later period of the disease as owing to their predilection for the endothelium of the blood vessel they invade the cytoplasm as well as the nuclei of these cells and are thus filtered out from the circulating blood. Cultivation of these organisms can be made only in the presence of living tissues and thus resemble viruses but they are unable to pass through fine bacterial filters.

Ricketsiæ pathogenic to man include the following:

(1) *Rickettsia prowazeki* da Rocha-Lima, 1916—The causative organism of epidemic typhus fever.

(2) *Rickettsia mooseri* (*muricola*) Monteiro, 1931—The causative organism of Brill's disease or endemic typhus.

(3) *Rickettsia rickettsi* Wolbach, 1919—The causative organism of Rocky mountain spotted fever.

(4) *Rickettsia orientalis* Nagayo *et al*, 1930—The causative organism of Japanese river fever or tsutsugamushi disease, pseudo-typhus of Formosa, scrub typhus of Federated Malay States.

(5) *Rickettsia burneti* Derrick, 1939—The causative organism of Q fever of Australia.

(6) *Rickettsia quintana var wolhynica*—The causative organism of trench fever. It is also transmitted by louse, *Pediculus humanus.*

Pathology—The specific reaction induced by rickettsial bodies is characterised by endothelial proliferation in the arterioles and perivascular infiltration with plasma cells and monocytes. These changes lead to vascular thrombosis followed by necrosis of tissues supplied by these vessels. This characteristic lesion is found in the vessels of skin, central nervous system and myocardium. Fraenkel (1914) first studied the specific histological lesion in typhus fever.

Transmission of Rickettsia bodies and mode of infection—The Rickettsia infections are transmitted to man by some arthropod vectors—a louse, a rat flea, a tick or a mite. Each of these insects are related to one specific Rickettsia. Louse carries *R. prowazeki,* rat flea carries *R. mooseri,* mite carries *R. orientalis,* tick carries *R. rickettsi.* Louse typhus is associated with famine, filth and overcrowding; hence epidemics of this type of typhus fever frequently follow war. The rest of the insect vectors are related to the sporadic outbreak of cases in certain localities and it has been assumed that they are communicated from certain natural reservoirs to man. This fact necessitated the search for an animal host which keeps up the infection in these endemic places. In some cases rodents play an important role as reservoir of infection, as in *R. mooseri and R. orientalis,* dogs and squirrels were found to be reservoirs of *R. rickettsi* in some places. There is no animal reservoir for *R. prowazeki* as man serves its reservoir host.

Cycle of Development in Arthropod Vectors—These arthropod vectors while feeding on infected patients during 3rd to 10th day of the disease ingest the rickettsia bodies along with their blood meal. On reaching the midgut of the insect they become intracellular parasites of intestinal epithelium. The organisms multiply inside these epithelial cells, ultimately the distended cells rupture and they become free in the lumen of the gut. They may either pass out with the faeces or proceed forward towards the proboscis when they are introduced into the puncture wound. In case of louse and rat flea the organisms are present in the faeces and the infection is conveyed by the contamination of the puncture wound caused by their bites with the infected faeces of these insects. The organism remains viable in dried faeces of lice for a period of 5 to 20 days and thus becomes a potential danger in spreading the infection to man and also to lice. The danger of these dried faeces lies further in this that they are blown about in the air of the sick-room and laboratory and thus contaminate the skin and mucous membrane of eyes and nose. Its viability in the underwear was found to be 10 days and under the finger nails as 4 days (Pshenichnov, 1942). The arthropod vectors do not as a rule become infected until a latent period of about 3 to 7 days has elapsed after the infecting meal. The infection in louse causes its death in 10 days whereas in case of rat fleas they are not in anyway affected by the rickettsial infection. The development in tick and mite is the same as that in louse but they show a widespread infection involving the gut, salivary glands, reproductive organs, brain and muscles. Rickettsiae are also found in the ova of infected tick and mite which are transferred to next

generations in large numbers. Further, the infection in these cases is conveyed by their bites (salivary gland infection) and both adult and larval forms are able to transfer the infection to man by their bites. It has been mentioned that as the infection is transmitted to their offspring, no animal reservoir appears to be necessary for maintaining the infection in the endemic areas.

Relation of endemic and epidemic typhus—In endemic typhus the main reservoir of infection is the rat and the infection is passed from rat to rat by a rat-louse (*Polyplax spinulosus*) which does not infest man and also by a rat-flea (*Xenopsylla cheopis*); the latter however infests man. It has been shown that under certain circumstances the human louse may also be infected with this Rickettsia (*R. mooseri*) and the cycle becomes thus changed, leading to the occurrence of an epidemic louse typhus. Thus the flea typhus occurs as sporadic and endemic cases where man lives in close association with rats and as the Rickettsia does not kill the rat, rat-flea and rat-louse, the infection survives in that particular locality. Thus it appears that the endemic typhus is an older disease which keeps up the infection and when epidemiological conditions are favourable it gives rise to an epidemic outbreak of the disease. Moreover the passage of the virus through rodents seems to lower its virulence and the disease when contracted first from these rodents, is generally of a milder nature but its passage through man often increases its virulence and when it spreads from man to man the percentage of mortality increases.

Serological Reaction—Agglutination with *B. Proteus* (Wilson-Weil-Felix Test)—Wilson (1909) isolated a proteus-like organism from the stools of typhus patients which gave an agglutination reaction with sera of the infected. Weil and Felix (1916) obtained a special strain of *Proteus vulgaris* (X bacillus) which gave a high agglutination titre with sera of patients suffering from epidemic typhus and since then the test is used as a diagnostic aid for typhus group of fevers. The test thus comes to be known as Wilson-Weil-Felix reaction. *Proteus X* bacillus produces indol in peptone solution and acid and gas in glucose, maltose and saccharose but not in lactose or mannite. There are different strains of this *Proteus X* bacilli and are designated as *X 19, X 2* and *X K*. It is worthy of note that only O variants of the culture are used and hence the prefix O *e.g., OX 19, OX 2* and *OX K*. These organisms have been isolated from blood, stool and urine of typhus patients but bear no etiological relationship with the disease.

The strain *X 2* was first obtained by Felix in 1915 from the blood of a patient suffering from typhus fever and *X 19* was isolated later. The strains *X 2* and *X 19* cannot be differentiated by any biochemical reaction as both produce indol in peptone water. The difference, however, lies in their O antigen and identification is possible only by cross agglutination. The strain *X K* or Kingsbury strain, differs from *X 19* in not producing indol in peptone water. It was originally an *X 19* strain and changed its character on keeping. Dr. Kingsbury obtained it from Lister Institute in 1921 and took it to Kaula Lumpur of Federated Malaya States.

In the serological reaction of typhus group of fevers all the three strains of *Proteus X* bacilli are put up and a macroscopic method is applied. Agglutinins appear in the blood of typhus patients after the end of the first week and the titre gradually rises during the course of the disease, the maximum reaction being obtained during convalescence after which it gradually declines and returns to negative from 6 weeks to 3 months after the onset of illness. A rising titre of over 1 in 100 should be taken as diagnostic for clinical purposes. Control reactions in other diseases do not exceed 1 in 50. This agglutination reaction appears to be non-specific in character. Satisfactory explanation cannot be given for such a non-specific reaction to be utilised for diagnostic purposes. Castaneda and Zia (1933) demonstrated by cross agglutination and absorption test a common antigenic factor (carbohydrate) in *Proteus X 19* and Mexican Rickettsiae which explains the principle involved in the Wilson-Weil-Felix reaction.

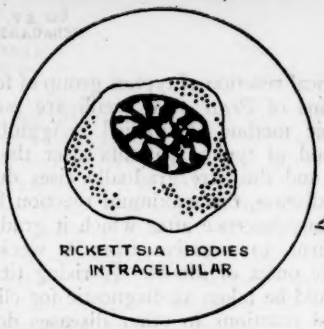
A serological differentiation with different strains of *Proteus X* bacilli has been noted in various group of typhus fevers as follows:—

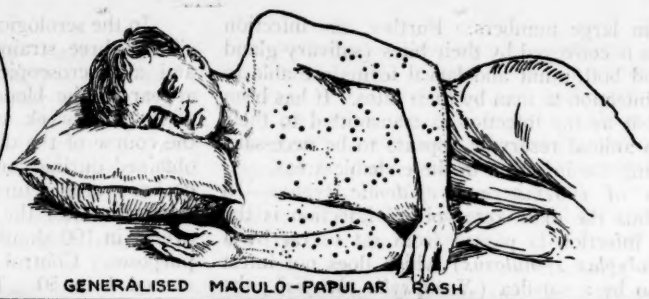
1. Agglutination with *OX 19* in high dilution is distinctive of louse-typhus (*R. prowazeki*) and flea-typhus (*R. mooseri*).
2. Agglutination with *OX K* only is distinctive of mite typhus (*R. orientalis*).
3. Agglutination with *OX 2, OX 19* and *OX K* in moderate dilution is distinctive of tick-typhus (*R. rickettsi*).
4. A negative reaction is distinctive of Q fever of Australia (*R. burneti*).

5. A schematic diagram (Fig. 1) is given to show the general features of the disease with their respective vector-reservoir-transmission and serological differences.

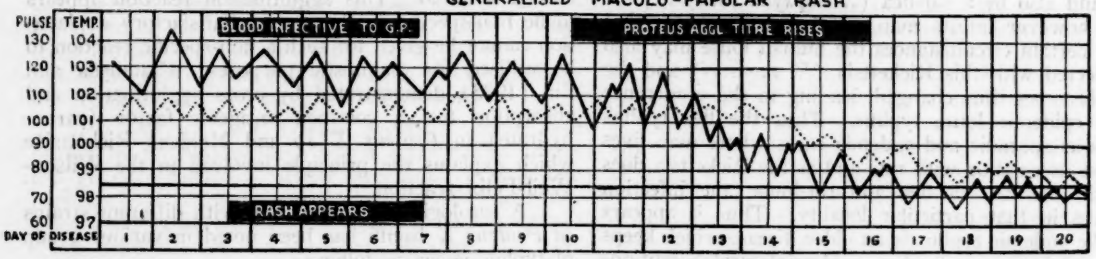
Animal Inoculation Test—Of all the laboratory animals, the guineapig is the animal of choice. The technique consists of an intra-peritoneal injection into a male guineapig of about 5 c.c. of infected blood (citrated) from a patient during febrile period. Reaction varies with different strains of Rickettsia. When the infection is with *R. prowazeki* there occurs a rise of temperature without any tunica vaginalis reaction after an incubation period of 6 to 14 days. Occasionally there is no febrile reaction and the virus is concentrated in the brain. In such cases an emulsion of the brain of the first guineapig when inoculated to a second guineapig will produce the characteristic fever. In infected guineapigs the organisms are also found in large numbers in the substance of spleen. With *Rickettsia mooseri* infection the animal shows a rise of temperature and scrotal swelling after an incubation period of 4 to 6 days. It was Neill (1917) who first observed the scrotal and testicular reaction while working with Mexican typhus. Rickettsia bodies can be demonstrated inside the endothelial cells of the exudate from tunica vaginalis; these are sometimes known as Mooser bodies (1928). The whole reaction thus came to be known as Neill-Mooser reaction. The scrotal reaction distinguishes *R. mooseri* from *R. prowazeki* but some doubt has been raised as this re-

TYPHUS GROUP OF FEVERS



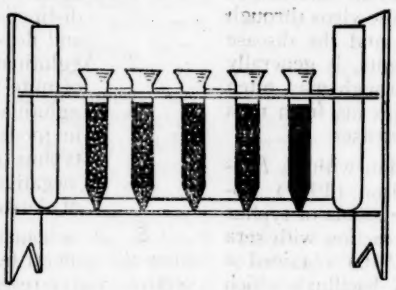


GENERALISED MACULO-PAPULAR RASH



TEMPERATURE CHART OF TYPHUS FEVER

SEROLOGICAL DIAGNOSIS



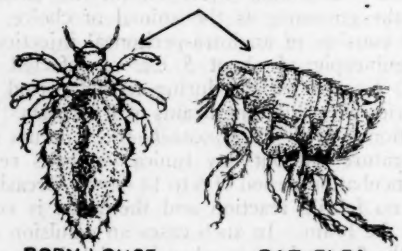
WILSON-WEIL-FELIX TEST. AGGLUTINATION REACTION WITH SERA OF TYPHUS PATIENTS WITH *B. PROTEUS* OX19, OX2 & OXK.

ARTHROPOD VECTORS

TYPE OX19
(OX19 ++ TO +++, OX2 +, OXK −)

TYPE OXK
(OXK++ TO +++, OX19− ; OX2 −)

TYPE *UNDETERMINED*
(OXK+, OX19+, OX2+)



BODY LOUSE
(*PEDICULUS HUMANUS*) CORPORIS

RAT FLEA
(*XENOPSYLLA CHEOPIS*)

MITE
(*TROMBICULA AKAMUSHI*)

TICK
(*DERMACENTOR ANDERSONI*)

RESERVOIRS OF INFECTION

FIG. 1 (Details in text)

action is occasionally observed with the latter. Another differentiating point between the two strains is that *R. mooseri* is more virulent for the rats than *R. prowazeki*. It is interesting to note that the sera of these infected guineapigs do not react with the Proteus bacilli. In mouse and rabbit a silent infection is produced but the sera of these animals react with Proteus bacilli. Intraperitoneal inoculation of *R. rickettsi* (the organism of Rockey mountain spotted fever) into young male guineapig causes a febrile reaction within 2 to 4 days, associated with swelling and haemorrhages in the scrotum. Guineapigs are refractive to *R. orientalis* (the organism of Tsutsugamushi fever); but when the organism is inoculated into the anterior chamber of the eye of a rabbit, it causes an acute inflammation and rickettsial bodies can be demonstrated in Descemet's membrane.

Chief Differentiating Features of Various Rickettsiae

1. *Rickettsia prowazeki* da Rocha-Lima, 1916 causes epidemic typhus fever. It is louse-borne and is transmitted to man by the infected excreta of the insect (*Pediculus humanus var corporis*). The serum of patients gives a positive Wilson-Weil-Felix reaction against *B. proteus OX 19*. Experimental inoculation in young male guineapig produces a febrile reaction without any scrotal swelling. Healthy human carriers probably serve as reservoir of infection.

2. *Rickettsia mooseri* Monteiro, 1931 causes endemic typhus or murine typhus or Brill's disease. It is flea-borne being transmitted from rat to rat and from rat to man by the rat flea, *Xenopsylla cheopis*. Infection in man is not introduced by the flea-bite. The serum of patients gives a positive Wilson-Weil-Felix reaction against *B. proteus OX 19*. Experimental inoculation into young male guineapig causes a testicular reaction and the Rickettsia bodies can be demonstrated in the endothelial cells of the exudate from tunica vaginalis. Rat louse is also capable of transmitting the infection from rat to rat but the rat louse does not bite man. Murine hosts are the reservoirs of infection.

3. *Rickettsia orientalis* Nagawo and others, 1930 causes Japanese river fever or Tsutsugamushi disease (tsutsugamushi is the Japanese name of a mite): pseudotyphus of Formosa; scrub typhus of Federated Malaya States. It is transmitted by a mite, *Trombicula akamushi*. There is often a sore at the site of the bite of mite with regional lymphangitis and lymphadenitis. The serum of patients suffering from this disease gives a positive Wilson-Weil-Felix reactions against *B. proteus OX K* only in high dilutions. Guineapigs are refractory when experimentally inoculated with the infected blood. The reservoirs of infection include rats and field voles.

4. *Rickettsia rickettsi* Wolbach, 1919 causes Rocky mountain spotted fever. It is transmitted by the bite of a tick, *Dermacentor andersoni* and a primary sore may develop at the site of the bite. The serum of patients gives a positive Wilson-Weil-Felix reaction against *B. proteus OX 19, OX 2,* and *OX K* in moderate dilution. Experimental inoculation into guineapigs causes a febrile reaction and occasional testicular reaction. The Rickettsia bodies invade the nucleus of the cell in contra-distinction with other Rickettsiae which are found inside the cytoplasm of the cell.

5. *Rickettsia burneti* Derrick, 1939 causes 'Q' fever in Australia. It is transmitted by a tick. The serum of patients suffering from the disease does not give a positive Wilson-Weil-Felix reaction against *B. Proteus X* strains. With specific rickettsial suspension a positive agglutination reaction is obtained.

Classification

Classification of typhus group of fevers was always a vexed problem. The various ways in which such classification may be based depend on the nature of the infecting Rickettsiae, the distribution of the disease on a geographical basis, the type of the transmitting

Table 1—Showing the Main Differences between Typhus Group of Fevers

	Epidemic typhus fever	*Endemic typhus fever*	*Tsutsugamushi disease, Japanese river fever*	*Rocky mountain spotted fever*
Synonym	Typus exanthematicus Louse typhus	Murine typhus Brill's disease, flea typhus	Tropical typhus, mite typhus, scrub typhus	Tick typhus.
Distribution	Mostly in European countries	World wide (mostly in tropical & sub-tropical countries	Japan, F.M.S.	U.S.A.
Infective agent	*R. prowazeki*	*R. mooseri*	*R. orientalis*	*R. rickettsi*
Anthropod vector	Pediculus humanus corporis	Xenopsylla cheopis	Trombicula akamushi	Dermacentor andersoni
Reservoir of infection	Man	Rats	Rats & field voles.	Dogs, squirrels
Rash	Appears on 3rd to 5th day; avoids face, soles and palms. Petechial tendency	Appears on 5th day; avoids face soles & palms. Petechial tendency	Appears on 7th day; on face, trunk & extremeties never petechial.	On 2nd to 5th day; widespread affecting face, soles & palms
Local sore & lymphadenitis	Not present	Not present	Often present.	May be present
Wilson-Weil-Felix test	OX 19 ++ to +++ OX 2 + OX K −	OX 19 ++ to +++ OX K − OX 2 +	OX 19 − OX 2 − OX K ++ to +++	OX 19 + OX 2 + OX K +
Guineapig inoculation test	Febrile reaction only	Fever and testicular reaction	Animal appears to be refractory	Fever & scrotal reaction

arthropod vectors and the nature of agglutination reaction of the sera of patients with *OX 2, OX 19* and *OX K* strains of *B. proteus*. Attempts was made to classify them on a vector basis but it was found that in many cases the vectors remained unknown or not clearly understood. The classification which is so widely advocated includes both the epidemiological factor and the transmitting arthropod vectors.

TYPHUS GROUP OF FEVERS

- Epidemic typhus (Typhus exanthematicus)
  - Louse typhus.
- Endemic typhus
  - Flea typhus (Murine typhus)
  - Mite typhus (Tsutsugamushi)
  - Tick typhus (Rocky mountain spotted fever)

The only scientific way would have been to classify them on an etiological basis but the isolation of Rickettsial bodies from human cases was not always attended with success. Further, introduction of specific Rickettsial emulsion in place of *B. proteus* for carrying out the Wilson-Weil-Felix test will go a long way to solve the problem. A considerable advance has no doubt been made regarding the immunological relationship of various Rickettsial infections with *B. proteus* which had greatly helped the diagnosis of the typhus group of fevers by Wilson-Weil-Felix reaction. On the nature of this serological behaviour, Felix (1935) divided them into three main subgroups as follows:—

(1) *Type OX 19* where agglutination response with 3 strains of *B. proteus* shows a positive reaction with *OX 19* in high dilution and negative for *OX K* (*OX 19* ++ to +++, *OX 2* +, *OX K* —). This includes two main groups.

(*a*) Epidemic typhus or louse typhus.

(*b*) Endemic typhus, murine typhus or flea typhus.

(2) *Type OX K* where agglutination response with three strains of *B. proteus* shows a positive reaction with *OX K* in high dilution and negative for *OX 19* and *OX 2* (*OX K* ++ to +++, *OX 19* —, *OX 2* —). Mite typhus or Tsutsugamushi disease belongs to this type.

(3) *Type undetermined* where agglutination with *B. proteus* shows a positive reaction with all the 3 strains in moderate dilution (*OX 19* +, *OX 2* +, *OX K* +). This includes tick typhus, Rocky mountain spotted fever. Felix thinks that the strain forming the main antigen of tick typhus group has yet to be discovered.

Diagnosis

A disease characterised by a high remittent or continued type of temperature with a widespread maculopapular rash appearing on 3rd to 5th day of the disease having a petechial tendency, a stuporous state, a comparatively slow pulse, moderate leucocytosis, a negative Widal reaction and the temperature coming down to normal within 3 weeks is included under the group of typhus fever. A local sore and lymphadenitis often appears to be a common feature of mite typhus and less so in tick typhus. The best way to confirm the diagnosis is to isolate the Rickettsia bodies from the blood of infected patient for which guineapig inoculation test is done. The febrile reaction, scrotal swelling and demonstration of Rickettsia bodies may place the diagnosis on a surer basis but the results are very variable. Equally satisfactory aid is obtained by Wilson-Weil-Felix non-specific agglutination test with strains of *B. proteus OX 19, OX K and OX 2*. Recently specific Rickettsial emulsions are employed as antigens for the agglutination test. It should be noted that the type of the disease and vector problem may also be suggested from the nature of the agglutination reaction. Skin biopsy is sometimes resorted to for diagnosis as when such sections are examined histologically the specific lesion, periarteritis nodosa due to thrombosis of smaller vessels are observed. Kamal and Messih (1943) reported an intradermal skin test which was found to be of great diagnostic value. They used 0·2 c.c. of saline suspension of *Proteus OX 19* (a loopful of 24 hours' culture suspended in 20 c.c. saline and killed by heat). In normal persons it caused an indurated area of erythema after 12 to 16 hours whereas in typhus patients there was no reaction.

Therapeutic Consideration

No specific treatment has yet been advanced for typhus fever and the patient is to be treated mainly for the symptoms and complication that may arise in the course of the disease. Good nursing thus forms an essential part of the treatment. Convalescent serum in doses of 20 to 30 c.c. were used but the result was disappointing. Although there are conflicting reports about the degree of usefulness and any specific protective action of the anti-serum but many workers have recommended the use of it for the treatment of the disease. With the improved technique in the preparation of Rickettsial vaccines, anti-serum may be produced on a large scale to be utilised for therapeutic purposes. Chemotherapy with various arsenicals and sulphonamides were tried in the past but no convincing result was obtained. Van Meerendonk (1942) reported good results with atebrin in a series of 225 cases of typhus fever where he was able to reduce the expected mortality to one-third but sufficient proof was not adduced to show that the drug had any destructive effect on Rickettsiae. Meerendonk *loc. cit* further observed a reduction of blood calcium as low as 6 mgm. per 100 c.c. in typhus fever and administration of calcium in such cases was found to give better results. The primary steps for prevention consist in measures taken against the various arthropod insects known to transmit the disease. In recent years considerable progress has been made in preparing prophylactic vaccines from diverse sources. Weigel (1924) in Poland first

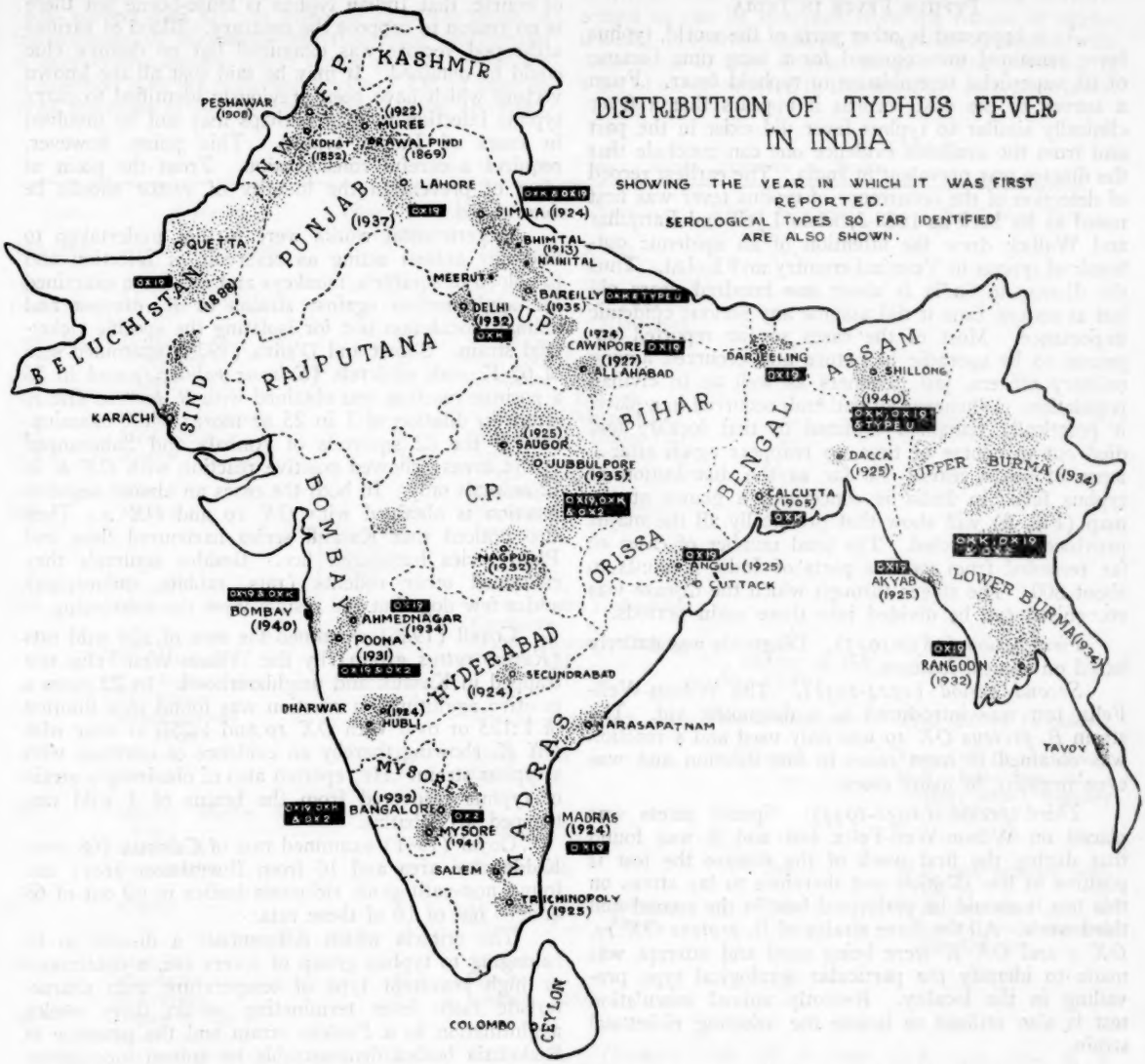


FIG. 2

made a vaccine from the intestinal contents of infected lice but this method cannot be applied on a large scale, as to protect one individual, material is required from 100 to 200 lice.

Owing to the antigenic relationship between murine typhus and epidemic typhus and also of the probable existence of a cross immunity, suspension of murine rickettsiae was also used for immunising purposes. Attempts were also made to find suitable methods for preparation of vaccines against epidemic typhus fever and the following procedures are now adopted:—

(1) Agar-slant tissue culture of Zinseer (1937).
(2) Yolk-sac method of Cox (1938).
(3) Mouse-lung method of Durand and Sparrow (1940).

In Rocky mountain spotted fever, prophylactic vaccine consists of a carbolised emulsion of heavily infected ticks. In tsutsugamushi disease, vaccine consists of formolised saline emulsion of blood or tissue from patients or infected animals.

Penicillin has recently been found to be effective in experimental murine typhus infection in mice by Moragues, Pinkerton and Greiff (1944) and therefore it may be used in cases of human typhus with success. As the laboratory infections are easily acquired, in the preparation of vaccine special care should be taken to protect the individuals who handle these materials. Owing to the infective nature of the disease a quarantine period of 15 days for immediate contacts has been advised.

Typhus Fever in India

As it happened in other parts of the world, typhus fever remained unrecognised for a long time because of its superficial resemblance to typhoid fever. From a survey of the past records it appears that a fever clinically similar to typhus fever did exist in the past and from the available evidence one can conclude that the disease was prevalent in India. The earliest record of detection of the occurrence of typhus fever was first noted as far back as 1852-3, when Lyell and Farquhar and Wallick drew the attention of an epidemic outbreak of typhus in Yusufzai country and Kohat. Thus the disease in India is about one hundred years old but at no one time it did assume any serious epidemic importance. Most of the cases so far reported appeared to be sporadic in nature and occurred among military officers, jail prisoners as well as in civilian population. Whenever an outbreak occurred in a place, it practically remained confined to that locality and died out in course of time, to reappear again after a lapse of some years. So far as the distribution of typhus fever in India is concerned, a glance at the map (Fig. 2) will show that practically all the major provinces are affected. The total number of cases so far recorded from various parts of India amounts to about 800. The stages through which the disease was recognised can be divided into three main periods.

First period (*1852-1923*). Diagnosis was entirely based on clinical features.

Second period (*1924-1931*). The Wilson-Weil-Felix test was introduced as a diagnostic aid. The strain *B. proteus OX 19* was only used and a reaction was obtained in most cases in low dilution and was even negative in many cases.

Third period (*1932-1944*). Special stress was placed on Wilson-Weil-Felix test and it was found that during the first week of the disease the test is positive in low dilution and therefore to lay stress on this test it should be performed best in the second and third week. All the three strains of *B. proteus OX 19, OX 2* and *OX K* were being used and attempt was made to identify the particular serological type prevailing in the locality. Recently animal inoculation test is also utilised to isolate the infecting rickettsial strain.

The vector problem has engaged attention because the clinical picture varies according to the vector and the virus may probably be modified by the vector which transmits the disease. All the arthropod vectors known to transmit the disease were incriminated from time to time, mostly by analogy and a guess from the serological diagnosis. While on other occasions, which are very few in number, the type of vector was suggested from a history of an insect-bite or a casual finding of a tick and a louse from the body of the patient. Again a mite and a rat flea was suspected on analogy because of their serological resemblance to the recognised types of disease. One fact which stands out pre-eminently was that an attempt was made to eliminate louse practically on epidemiological and social grounds, but no prima facie case has yet been made to exclude it altogether. It has not been proved, of course, that Indian typhus is louse-borne but there is no reason to suppose the contrary. Blood of various arthropod vectors was examined but no definite clue could be obtained. It may be said that all the known vectors which have been previously identified to carry typhus infection to man perhaps may not be involved in cases of Indian typhus. This point, however, requires a careful consideration. From the point of view of prevention the identity of vector should be determined.

Experimental works were further undertaken to find any animal acting as reservoir of infection and the blood of squirrels, monkeys and rats were examined for agglutination against strains of *B. proteus* and animal inoculation test for isolating the specific rickettsial strain. Shortt and D'silva (1936) examined sera of 65 Kasauli squirrels (*Sciurus palmaris*) and in 36 a positive reaction was obtained with *B. proteus OX K* strain in dilution of 1 in 25 or more; while examination of the 62 squirrels of Ambala and Saharanpur (plain areas) showed positive reaction with *OX K* in 12 animals only. In both the cases an almost negative reaction is obtained with *OX 19* and *OX 2*. They also noticed that Kasauli series harboured fleas and Plain series harboured lice. Besides squirrels they examined other rodents (rats, rabbits, guineapigs) and a few dogs but the results were not convincing.

Covell (1936) examined the sera of 524 wild rats (*Rattus rattus* group) by the Wilson-Weil-Felix test trapped in Kasauli and neighbourhood. In 22 cases a positive agglutination reaction was found in a dilution of 1:125 or over with *OX 19* and 1:250 or over with *OX K*, showing thereby an evidence of infection with a typhus strain. He reported also of obtaining a strain of typhus recovered from the brains of 3 wild rats trapped at Sabathu.

Goyal (1941) examined rats of Calcutta (68 from Kidderpore area and 16 from Burrabazar area) and found non-pathogenic rickettsia bodies in 60 out of 68 and 10 out of 16 of these rats.

The criteria which differentiate a disease to be belonging to typhus group of fevers are, a continuous or high remittent type of temperature with characteristic rash, fever terminating within three weeks, agglutination to a *Proteus* strain and the presence of Rickettsia bodies demonstrable by animal inoculation. It is not possible to get all these manifestations in every individual case but if one obtains a positive Wilson-Weil-Felix test or a positive animal inoculation test (fever with or without Neill-Mooser reaction), it puts the diagnosis of the disease on a firmer basis. But many cases are on record where only a fever and typical rash have made the disease to be labelled as typhus fever. Then again there are cases on record where the disease was diagnosed even in the absence of the characteristic rash by Wilson-Weil-Felix test. Isloation of Rickettsia bodies from a case of typhus fever will no doubt be the most accurate scientific method for identification of the disease. Typhus fever has now come to be recognised to have a cosmopolitan distribution but a number of local forms or varieties have been distinguished which, however, is the result of existing local conditions having a remarkable

influence on the arthropod intermediary hosts. In India correct data are not available as to the mode of transmission of Rickettsia infection from one person to another because the insect vector and the reservoirs of infection have yet remained unsolved. On an analysis of all the cases of Indian typhus fever so far recorded, it will be seen that each of the major groups is represented as can be observed from the nature of agglutinating properties against *B. proteus X* strains with differences in their clinical picture. The following is a list of cases reported in the literature as typhus fever. (Table 2).

TABLE 2—SHOWING THE CASES OF TYPHUS FEVER REPORTED IN INDIA

Year.	*Reported by*	*Number of cases*	*Place of occurrence*	*Vector suggested*	*Serological Test*
1852-1853	Lyell & Farquhar, Wallick	..	Yusufzai & Kohat	..	..
1869	Fairweather	..	Rawalpindi Jail	..	..
1888-1894	Hendley, Pisani	..	Beluchistan to Yusufzai & Hazara; Himalayan hill tracts (Kulu)	..	..
1905-1906	Husband & Mc-Watters	120	Northern India	..	..
1908	Hepper	6	Peshawar Jail	..	..
1905-1912	Mitra	21	Calcutta & Howrah	..	..
1912	Bradley & Smith	1	Calcutta (Barrackpore)	..	..
1913	McKechnie	30	Kumaon hills (Bhim Tal)	..	..
1917	Megaw	1	Lucknow (contracted from Bhim Tal)	Tick	..
1917	Mitra	3	Calcutta	..	..
1921	Megaw	5 (3 Chapman 1 Hardy 1 Sprawson)	Nagpur, Cawnpore, Bangalore	Tick	..
1922	Keates	1	Murree	..	..
1924	Megaw	5	Central India, Hyderabad, Cawnpore	..	..
	Jackson	5	Hubli, Dharwar, Gadgag	..	..
	Williamson	1	Saugar, C.P.	No. history of tick bite (Tick)	..
	Cunningham & Theodore; Krishnaswamy (1928)	8	Madras Presidency	Vector unknown	Type OX 19 (1 case)
	Phipson	16	Simla Hills	Louse	Type OX 19 (12 cases)
	Basu	15	Calcutta	..	W.F. test done in 3 cases; result negative with OX 19
1925	Megaw, Shettle & Roy	9	Saugar, C.P.	..	..
	Norman & Ramchandra	1	Trichinopoly	Tick	W.F. test negative with OX 19
1925	Megaw	7	Orissa, Dacca, Balaghat, Saugar (C.I.) Akyab	Tick	W.F. test done only in 2 cases result negative with OX 19
1927	Banerjee	1	Allahabad,	..	..
	Mackenzie	2	Hazara	..	..
	McWatters	2	Kumaon Hills	..	..
1928	Megaw & Rao (cases collected by several doctors)	55	C.I., C.P., (Saugor) Bangalore, Peshwar, Nainital, Kumaon Hills, Darjeeling	Tick (3) & louse (2) in 5 cases; rest vector unknown	W.F. test done in 5 cases; result negative
	Ghosh	3	Allahabad	History of some insect bite	Not done
1929	Thomson	7	Dehra Dun	..	W.F. test positive in low dilution (1:40)
1930	De	1	Bilaspur	..	..
1931	Pai	2	Poona	..	W.F. test negative
1932	Biggam	3	Bangalore	Vector unknown	Type OX K—1 case Type OX 19— 1 case
	Christian	1	Delhi	Tick	Type OX K
	Mukherjee	4	Nagpur	History of tick bite in 1	W.F. test negative
	Kundu	1	Rangoon	..	Type OX 19
1933	Martin & Anderson	1	Burma	History of insect bite	Type OX K
1934	Lindeman	2	Karachi & Quetta	Nil	Type OX 19
	Blewitt	21 (8 cases in 1932 & 13 „ in 1933)	Ahmednagar	Tick bite in 2 cases	Type OX 19

Year.	*Reported by*	*Number of cases*	*Place of occurrence*	*Vector suggested*	*Serological Test*
1935	Boyd	43	Northern, Eastern & Southern commands	Vector unknown	Type OX K
		14	Deccan Dists. & Poona	Vector unknown	Type OX 2
		51	Poona-Ahmednagar & Bangalore	Vector unknown	Type OX 19
	Macnamara	16	Simla Hills	Vector unknown	Type OX K
		19 (5+14) (in 1932-33)	Simla Hills	..	..
	Christian	6	Bareilly (U.P.)	..	Type OX K (1) Type undetermined (5)
	Sachs	7	Jubbulpore (5) Bareilly (1) Peshawar (1)	History of tick bite in one.	Type OX 19
	Wilson	1	Rangoon (contracted from Calcutta)	..	Type OX K
1935	Stott	1	Lucknow	Vector unknown	Type OX 19
1936	Covell	5	Simla	Rat flea, louse	Type OX K & OX 19
1936	Curran	10	Jubbulpore	Vector unknown	OX K, OX 19, OX 2
1934-1936	Maitra & Sen Gupta	109	Upper & Lower Burma	..	Type OX K (40) Type OX 19 (66) Type OX 2 (3)
1937	Banerjee	1	Allahabad	..	..
	Yacob	8	Punjab (Muzaffargarh)	Mite	Type OX 19 W.F. test positive in low dilution (1/80)
	Kapila & Maitra	1	Burma (Bhamo)	..	Type OX K
	Hassett	1	Malakand	..	Type OX 19
1936-1938	Sharma	56 (12 out of 56 showed rash)	Bangalore	Vector unidentified (Tick)	Type OX 19 (50) Type OX 2 (5) Type OX K (1)
1940	Patel, T.B.	15 & 1 in each year of 1917, 1932, 1933, 1937.	Bombay	Rat fleas	Type OX 19
1941-1942	Heilig & Naidu	14	Mysore	Vector undetermined	Type OX 2
1940-1941	Woodhead & Dutta	17	Assam	Mite, Rat flea, tick	Type OX K (8) Type OX 19 (6) Type undetermined (3)
1941-1942	Bombay Health Officer	13	Bombay	Louse or tick	Type OX 19 & OX K
1942	Soni	3	Burma	..	Type OX 19
	Napier	16	Calcutta	Vector unknown	Majority Type OX K
	Patel, N.D.	1	Bombay	..	Type OX 19 & OX K
	Patel, B.R.	1	Mysore	..	..
1943	Patel, J.C.	6 (no rash seen)	Bombay	Rat flea	Type OX 19 (5) Type OX K (1)
	Patel, N.D.	6	Bombay	Rat flea	Type OX 19 & OX K
	Singh	1	Meerut (Delhi)	Tick	W.F. test negative

Typhus Fever in Calcutta

The occurrence of typhus fever amongst the military officers stationed at Calcutta and its neighbouring areas was reported by various observers from time to time. Bradley and Smith (1912) recorded a curious case of fever in Calcutta (near Barrackpore) which was diagnosed on clinical grounds as typhus fever. Boyd (1935) while reporting on cases of typhus fevers in India observed some cases amongst officers stationed at Calcutta. Wilson (1936) reported a case of typhus fever from Rangoon the infection being contracted when the officer was in Calcutta. The case resembled Malayan tropical typhus as the serum reacted with *B. proteus OX K* in dilution of 1:2500. The vector remained unknown. Napier (1943) reported the occurrence of an outbreak of typhus fever amongst the British soldiers in Calcutta in autumn of 1942. There were altogether 16 cases with 2 deaths. The serum in all the cases gave a positive reaction with *B. proteus OX K* except one which reacted with *B. proteus OX 2*. In these cases also the nature of the arthropod vectors remained unknown.

Incidence of typhus fever amongst the civilian population in Calcutta were less frequent, as compared with other parts of India. There were only a scanty reference of the disease in the literature. Mitra (1912) collected 21 cases of typhus fever from the year 1905 to 1912 occurring in Howrah and Calcutta. Diagnosis was entirely based on clinical observations and the mortality was observed to be 50 per cent. Mitra (1917) reported another 3 cases of typhus fever occurring in Calcutta. Basu (1925) gave an account of 15 cases of exanthematic typhus and only in three cases Wilson-Weil-Felix test was done but the results were all negative. Two cases are reported here. In one of them an opportunity was obtained for carrying out a detailed laboratory investigation and the disease

was confirmed by agglutination with Proteus strain of bacillus and by animal inoculation test.

Case Reports

Case No. 1—H. F. aged 52 years resident of South Calcutta had an attack of sudden onset of fever (101°F) with headache and pains all over the body. The fever was ranging from 101° to 104°F. On the 5th day of her illness she developed a roseolar eruption which appeared first on the face and then gradually spread all over the body and limbs affecting even the palms of hands and soles of the feet. All the eruptions appeared by the 7th day of her illness and maculo-papular in character becoming petechial on the 10th day of her illness. The eruption all persisted till death which occurred on the 14th day of her illness. Face and eyes were congested. Nervous system was involved early. The patient was stuporose by the 3rd day. Pulse rate was ranging from 100 to 110 per minute in the beginning and was regular. Tongue was dry and coated with brown fur. Bowel was constipated. Liver and spleen were not palpable. On the 10th day of her illness the patient had pneumonic consolidation affecting both the lungs. Respiration became hurried (60 per minute), pulse rate increased (130 per minute). She became semiconscious and began to pass urine and stool involuntarily. She died of acute circulatory failure on the 14th day of her illness.

The patient lived in healthy surroundings and in good hygienic conditions. Her habits were clean. There was no history of staying outside or contact with any people other than her family members. She was staying for the last 2 years in her residence in Calcutta.

Laboratory investigation—Blood picture showed: —Hb. 65 per cent, R.B.C.—3·4 millions, W.B.C.—11,250 per c.mm. with a differential count of poly 85 per cent, lympho 15 per cent, mono nil, eosin nil. Widal reaction negative to *B. typhosus, para A and B*. Wilson-Weil-Felix test was not done.

Comment—From the clinical features the case may be labelled as typhus fever as she was having a high remittent temperature with characteristic rash on the 5th day, moderate leucocytosis and negative Widal reaction. The distribution of rash resembled that of Rocky mountain spotted fever. Death was due to pneumonic complication. As Wilson-Weil-Felix test was not done, serological type cannot be ascertained. The insect vector remained unknown.

Case No. 2—H. M. aged 38 years, married, a resident of South Calcutta had an attack of sudden onset of fever with headache, general malaise and pain all over the body. The patient was running a continuous type of temperature ranging from 103° to 104°F. The pulse rate was moderately slow being 110 per minute with a temperature of 104°F. Spleen and liver were not palpable. Lungs were free. There was no abdominal distension and no tenderness in any area. Bowel was constipated. Tongue was coated with a brown fur. Eyes were congested. The patient lived in good healthy surroundings and his habits were clean. There was no history of any insect bite.

Towards the end of the first week the patient was unusually drowsy and there was marked prostration. On about the 9th day of the illness a rosy erythema was noticed on the abdomen and sides of the chest. Later it became maculopapular with subcuticular mottling and spread to the limbs. Face, neck, palms of hands and soles of feet were particularly free from the rash. With the appearance of the rash, the temperature however continued and the prostration was more marked. The patient was now almost in a comatose condition passing urine involuntarily. At times delirium was noticed. Towards the end of the second week, the temperature took an intermittent character and came down to normal by lysis, on about the 18th day of the disease. At this time the consciousness returned but the pulse rate was feeble and rapid and the first heart sound in the mitral area was weak and soft. Myocardial weakness persisted and on about the 21st day of the disease, the patient had an attack of circulatory failure (central and peripheral) and died of it.

Laboratory investigations—Blood examination done on 2-9-44 *i.e.*, on the 13th day of illness showed: —Hb. 67 per cent, R.B.C.—4,810,00 per c.mm., W.B.C.—6,250 per c.mm., poly 79 per cent, lympho 18 per cent, mono 1 per cent, eosin 2 per cent. Widal test against *B. typhosus, para A. and B* all showed a negative recation in 1:25 and higher dilutions.

Animal Inoculation Test—On 6-9-44 *i.e.*, the 17th day of illness, 5 c.c. of citrated blood was inoculated intraperitoneally into a male guineapig weighing 380 gms. After an incubation period of 4 days the temperature of the animal rose to 41·8°C. and remained so for 6 days. No testicular reaction was observed. The animal did not die. On 15-9-44 while the animal was running a temperature, about 3 c.c. of heart's blood from the infected guineapig was inoculated into a second male guineapig weighing 340 gms. which also showed a high temperature of 41°C. from the 6th day. The temperature came down to normal after remaining high for 2 days.

Serological Test—Wilson-Weil-Felix test was done on the 17th day of illness and the end titre was observed with different strains of *B. proteus*. The serum of the patient gave an agglutination with OX 19 in 1 in 2,500, with OX 2 in 1 in 125 and with OX K in 1 in 1250. OX 19 and OX K were formolised suspensions, whereas OX 2 was an alcoholised suspension.

Comment—The case was diagonised clinically as typhus fever and the laboratory investigations confirmed it. The agglutination reaction was not clear cut as it gave a positive reaction in high dilution both with OX 19 and OX K. Clinically the distribution of the rash conformed to OX 19 type. The vector problem remained unsolved.

Discussion

Two cases of typhus fever occurring among the civilian population are recorded. Both the cases were observed during the third week of August 1944, with an interval of 2 days. Only in one case the clinical diagnosis could be confirmed by animal inoculation test

and Wilson-Weil-Felix test. Clinically in one case the distribution of rash conformed to that of the Rocky mountain spotted fever but in this case the Wilson-Weil-Felix test was not done. In the second case the distribution of the rash conformed to that of louse typhus or flea typhus and the agglutination reaction was positive with *B. proteus OX 19* in high dilution (1 in 2500). But the only fallacy in this case was that the serum also reacted with *B. proteus OX K* in a dilution of 1 in 1250 which is contrary to the usual finding. The vector in both the cases remained unidentified. In this connection it may be pointed out that Dr. N. D. Patel from Bombay recorded a case in 1942, the serum of which agglutinated Proteus strain *OX 19* and *OX K* in high dilution (1 in 1000) on the 8th and 15th day of illness.

Summary

1. A brief description of typhus fever regarding its clinical features, bacteriology, pathology, transmitting arthropod vectors and laboratory investigations are given. A schematic diagram is given to show the evolution of the disease and its recognition.

2. Incidence of the cases of typhus fever in India is discussed and a table is given of all the cases, so far reported. A map of India showing distribution of typhus fever in India with the serological type prevailing in the locality and also the year in which the disease was first recognised is given in diagram.

3. The number of cases of typhus fever in Calcutta as appeared in the literature are analysed.

4. Two cases of typhus fever occurring amongst the civil population of Southern part of Calcutta are recorded. These cases cropped up during the month of August 1944. Both the cases were diagnosed clinically and only in one facilities could be obtained to confirm it by serological reaction and guineapig inoculation test. From the agglutination reaction it appeared that the disease resembled louse typhus or flea typhus as well as with that of scrub or mite typhus. Hence no conclusion can be derived as to the serological type.

The laboratory investigations were carried out in the Pathological laboratory of the Carmichael Medical College, Belgachia, Calcutta, and were confirmed by the Professor of Pathology, Dr. C. C. Basu, who also supplied the proteus strains of *OX K, OX 19* and *OX 2*.

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A FURTHER NOTE ON THE TREATMENT OF BLACK WATER FEVER WITH ANTIVENENE

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Singh and Singh (1944a) recorded thirty seven cases of black water fever, successfully treated with antivenene, which was found to act as an anti-hæmolytic *in vivo* as well as *in vitro*. It was concluded that even during an attack of black water fever antivenene might render safe the administration of anti-malarial drugs, which are otherwise apt to precipitate further hæmolysis. This theoretical likelihood was realised in practice (Singh and Singh, 1944b, 1945a) and four further cases were recorded in which during the attack of black water fever, mepacrine along with antivenene was administered in total dosage of 1·5 to 2·7 gm. to treat the causative malaria without any complication of fresh hæmolysis. In this paper is recorded a case in which during the attack of black water fever antivenene rendered safe the administration of not only mepacrine, but of a powerful combination of quinine and mepacrine in full doses, this combination having been found to be the most potent therapeutic agent against virulent and resistant strains of malarial parasites (Singh and Singh 1945b).

Case Record

Male aged 25, a resident of the Terai region of Nepal, had several inadequately treated attacks of malaria before, the last being eight months ago. He came under observation on 1-7-45, the fourth day of illness, complaining of continuous fever with intermittent rigors, bilious vomiting, diarrhœa without blood and mucus in the stools, and severe headache. A labourer in a pig farm by occupation, he went on his work as usual on the first day of his illness, but subsequently found himself too ill and remained confined to bed without any treatment.

On examination he was very ill, weak, debilitated, pale and covered with a cold clammy sweat. Pulse rate was 120 per minute with a blood pressure of 105/70 mm. of Hg., respiration 30 per minute, and temperature 99·6F. Tongue was dry and coated. The spleen was moderately enlarged and tender, and there were no other abnormal physical signs present.

Blood smear showed a heavy infection with M.T. rings and a few gametocytes. As many as 29 per cent of the red cells in the peripheral blood were infected and 10 per cent showed multiple infection with two and sometimes three parasites in a red blood cell. In the vast majority of them the rings were marginal forms. The red blood cell count was 4,980,000 per c.mm. of blood, and hæmoglobin was 13·8 gm. per cent. Stools and urine showed no abnormality.

Black water fever was precipitated on the third day of treatment after the administration of quinine bihydrochloride gr. 54, and mepacrine 0·425 gm. Hæmoglobin fell to 8·5 gm. per cent and the red blood cell to 3,200,000 per c.mm. of blood. Standard treatment for black water fever and pernicious forms of malaria, as advocated by Singh and Singh (1944a), was given. Antivenene, quinine, and mepacrine were given in the following dosage with progress as shown in Table I.

Table I.

Day	*Concentrated Antivenene*	*Mepacrine*	*Quinine*	*Blood*	*Temperature*	*Colour of urine*	*Remarks*
1.	Nil	0·125 gm. I.M.	6 gr. I.V. 12 gr. I.M.	M.T. rings 29 per cent.	99·6 F.	Normal	Very ill. Urine made strongly alkaline with alkalies by mouth.
2.	Nil	0·1 gm. t.d.s.	10 gr. t.d.s. 6 gr. I.V.	M.T. rings 14 per cent.	97·6-99·2F.	Normal	Very ill. One dose of quinine 10 gr. vomited.
3.	20 c.c. I.V. 10 c.c. I.M.	0·125 gm. I.M. 0·1 gm. t.d.s.	Nil	M.T. rings 2 per cent.	97·6-99F.	Very dark (oxyhæmoglobinuria)	Black water fever precipitated. Epileptiform convulsion.
4.	10 c.c. I.V. 10 c.c. I.M.	0·125 gm. I.M. 0·1 gm. B.D.	10 gr. t.d.s.	M. T. rings scanty.	97-99F.	Normal (No oxyhæmoglobinuria)	Serum also showed no oxyhæmoglobin. Frequent scanty stools with blood and mucus—bacillary exudate.
5.	Nil	0·125 gm. I.M. 0·1 gm. B.D.	10 gr. t.d.s.	Nil	97-99F.	Normal	Scanty stools with blood and mucus—bacillary exudate.
6.	Nil	0·1 gm. t.d.s.	10 gr. t.d.s.	Nil	96·8-98	Normal	Stools same as previous day. Sulphaguanidine course started.
7.	Nil	0·1 gm. t.d.s.	Nil	Nil	Normal	Normal	Marked improvement in dysenteric symptoms.
8.	Nil	0·1 gm. t.d.s.	Nil	Nil	Normal	Normal	Marked improvement in dysenteric symptoms.
9.	Nil	0·1 gm. t.d.s.	Nil	Nil	Normal	Normal	Stools normal. Sulphaguanidine stpoped.
10 & 11.	Nil	0·1 gm. t.d.s.	Nil	Nil	Normal	Normal	Convalescence satisfactory.

Discussion

The action of quinine in augmenting hæmolysis of red blood cells in black water fever is well known. It is one of the strongest predisposing factors and experimentally it is possible to provoke in many cases of black water fever a relapse with smallest doses of the drug. Methylene blue, phenacetin, antipyrin, salvarsans, and even irradiation of the spleen may at times appear to be responsible for precipitating black water fever, but such cases are extremely rare in comparison to those which occur following quinine. This is not exclusively due to the fact that quinine of them is the most widely used drug. Experimentally it has been shown by Kikuth and Nocht (1933), that hæmolytic amboceptors produced in rabbits by the injection of dog's blood exhibit an increased hæmolytic effect in the living subject (but not in the test-tube) if quinine is simultaneously or subsequently injected. It was found that small doses of hæmolytic amboceptors not enough to produce even a hæmoglobinæmia, when exhibited with quinine produced hæmoglobinæmia as well as hæmoglobinuria. It appears, therefore, that quinine is capable of suspending or at least considerably weakening the neutralising effect of anti-haemolysins in the animal organism.

In *in vitro* experiments using serum containing hæmolysins from black water fever cases it was found (Singh and Singh, 1944a) that traces of quinine 1 in 300, pamaquine 1 in 10,000 and mepacrine 1 in 500, accentuated the hæmolytic process. It would thus appear that quinine is at least six times as powerful as mepacrine and one-third as powerful as pamaquine in augmenting hæmolysis.

The precipitation of black water fever by mepacrine is infrequent, but nevertheless has been recorded by several observers, Manson-Bahr (1942), Foy and Kondy (1942), Rogers and Megaw (1942), Singh and Singh (1944a). Mepacrine does so in greater concentration, and hence black water fever seldom occurs with mepacrine.

The administration of quinine in larger doses during the black water stage when parasites persist has been dreaded and that of mepacrine somewhat guarded on account of their tendency in precipitating fresh attacks of hæmolysis. The results of treatment in this case however show that whenever indications exist for the administration of anti-malarial drugs, quinine and mepacrine can be administered singly, or even in combination, if need be to treat virulent and resistant strains of malarial parasites, along with antivenene with impunity.

Baker and Dodds (1942) found that animals passing an alkaline urine are not effected by injections of hæmoglobin, but if urine is made acid intrarenal obstruction follows. *In vitro* experiments show that hæmoglobin is precipitated as acid hæmatin when

(1) the reaction of the solution is not more than about *p*H 6, and

(2) the sodium chloride content is about one per cent (hence the value of treating anuria with infusions of hypertonic or isotonic glucose, rather than infusions of isotonic saline or glucose saline).

An interesting feature in relation to the above findings was noticed in this case in human beings. Although about two-fifths of the total number of red cells in the peripheral blood were hæmolysed, examination of urine and blood showed that the liberated hæmoglobin was completely eliminated within 10 hours without causing any anxiety about the kidneys. Ordinarily without prior alkalinisation if the cases progressed favourably with the routine treatment, it would have taken about 48 to 72 hours, or even more. In this case the urine had been rendered completely alkaline early during the treatment of malaria before black water fever was precipitated.

Summary and Conclusions

1. The clinical use of antivenene in the treatment of black water fever has been attended with success in one case.

2. The causative malaria was treated with full dosage of quinine and mepacrine combined, along with antivenene, without fresh hæmolysis.

3. Prior alkalinisation of urine during the treatment of the malarial infection, rendered elimination within 10 hours, of hæmoglobin liberated by hæmolysis of about two fifths of the red cells in the perepheral blood, when black water fever was precipitated. The early use of alkalies for rendering the urine alkaline, in the treatment of M.T. infections in which black water fever is likely, is therefore advocated.

Acknowledgment

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MATERNAL MORTALITY

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Introduction

40 deaths occurred in 1087 deliveries in Queen Mary's Hospital, Lucknow. The maternal mortality rate 38·8 per 1000 births is thus a very high figure as compared to 5 per 1000 births in European countries. The factors responsible are given below.

Table Showing Causes of Maternal Death

Sepsis		..	1
Eclampsia and toxæmia of pregnancy		..	4
Antepartum hæmorrhage ..		..	3
Postpartum hæmorrhage ..		..	6
After operation (Cæsarian) ..		..	4
Exhaustion and collapse ..		..	4
			22
Lung diseases			
—Tuberculosis	1		
—Pneumonia	3	..	4
Heart diseases		..	2
Renal disease		..	1
Paraplegia		..	1
Anæmia		..	4
Injury with hæmaturia ..		..	1
Unknown		..	5
			18
		Total ..	40

The analysis will show that postpartum hæmorrhage is responsible for 15 per cent of the total death. In three cases hæmorrhage was due to adherent placenta. A case of leprosy died after cæsarian section. In one case *peritonitis* followed the cæsarian operation. This case was admitted with foul discharge per vaginum and rags were taken out in the hospital from the vagina and uterus. Other 2 cases who died from postoperative complications of cæsarian section were of *osteomalacia.*

Exhaustion and collapse—These cases would have been saved if they had come to the wards earlier. All the cases were nearly exhausted before admission. Three cases developed septic *pneumonia.* One case was admitted with the history of not passing urine for seven days. The death most probably was due to *renal failure.*

The general nutrition of the cases was poor. Majority of them complained of constipation. Below is the relative incidence of the diseases associated with pregnancy.

Syphilis	8·2%
Gonococcal infection ..	2·0%
Diabetes and goitre ..	2·0%
Pyelitis and albuminuria ..	13·5%
Enteritis and dysentery ..	18·5%
Anæmia	34·5%
Osteomalacia	11·0%
Tuberculosis	8·0%
Injury and other diseases ..	3·2%

(*Continued at col. 2*)

EOSINOPHILIC PSEUDO-LEUKAEMIA

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This interesting condition of eosinophilia has recently attracted much attention in India and abroad. There is a controversy whether this eosinophilic condition of blood should be recognised as a disease entity or not. Various synonyms suggested by different observers show that they have different clinical, ætiological and pathological factors in their mind. Whether eosinophilic lung is a new disease which has been met with in practice during the last decade or two and is reported so often in medical literature or whether more frequent improved laboratory methods and radiological aid in diagnosing cases is responsible for bringing this condition into prominence remains to be seen. On going over blood reports of patients I have got from 1932 to 1944 I have not a single report which shows eosinophilia of more than 7 per cent. It is only in 1945 that eosinophilia of 85 per cent and 60 per cent was reported by the pathologist in my local practice.

I was much impressed by the dramatic relief brought about by six Neo-arsphenamine injections in one of these two cases. The other patient was lost sight of before the course of treatment was completed. I give below my notes on one of these cases.

Case Report

Mr. T. aged 26 years, lawyer, started trouble in November 1944 when he was out on a professional visit in a public bus. Road was dusty and he was sitting on the back seat of the vehicle. He believed that dust was responsible for causing this trouble which harassed him for six months, till at last he was relieved by neo-arsphenamine injections.

(*Continued from col. 1*)

The above diseases accounted for 6 per cent of all the cases. There is greater preponderence of anæmia and enteritis cases. Cases of malaria were few and negligible. One case suffered from beri beri and one was a case of leprosy out of the whole series.

(*Continued from page 146*)

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Family history—Father, his two brothers and sister are robust and healthy. Mother died of nephritis three years back. No history of asthma or tuberculosis in the family.

Previous history—Quite healthy and working with full vigour till he got this illness. Weight 130 lbs. before he fell ill.

When he consulted me on 25-3-45 he was looking emaciated and slightly anæmic. Weight 108 lbs. Temp. 98·2°F at 7 p.m. Pulse 98 p.m. He was complaining of spasmodic cough and low fever running between 98·4° and 99·5°F for five months. The father and son used to count number of spasms of cough in 24 hours which struck me most when I asked his history of illness. On physical examination percussion note was uniformly resonant and there was no prolongation of expiration. I could hear rhonchi and occasional rales in both lungs, but no fine crepitations could be heard. Patient did not complain of asthmatic breathing or spasms or of any dyspnœa. Hacking cough brought out only white mucoid substance. Liver and spleen were normal. There were no signs of dyspepsia. Urine was normal.

With a mild form of anæmia, with history of five months' illness without muco-purulent nummular sputum, with widespread abnormal sounds in both lungs attended with low fever my clinical diagnosis was chronic bronchitis with mild anæmia. The same impression was at first reported by the tuberculosis specialist who afterwards took his blood for examination. I quote his remarks verbatim:—"I cannot say definitely that it is a case of Lung T.B. There is a great probability of its being not T.B.". I am particularly mentioning this fact to show what first impression is produced by careful clinical examination of such patients. I gave him accordingly anti-catarrhal vaccine, calcium injections, A & D vitamins with glycerophosphates by mouth. He was sent to a tuberculosis specialist for examination as mentioned above whose blood report revealed the true nature of the case (19-4-1945):—

Neutrophils—10 per cent, eosinophils—85 per cent and lymphocytes—5 per cent.

This blood result put me on the right track. Here was a case of eosinophilic pseudo-leukæmia or eosinophilic lung. I gave him first neo-arsphenamine injection in 10 c.c. re-distilled water on 25-4-45 followed by five more injections. Last neo-arsphenamine injection was given on 29-5-45. After three injections I could distinctly see a definite change in his general appearance. He was much relieved of his cough. Rhonchi and rales disappeared. Temperature began to settle down to 97°F (armpit).

Blood report on 14-5-45 after third neo-arsphenamine injection was:—

White cells—no appreciable leucocytosis; differential count: Neutrophils—46 per cent, eosinophils—28 per cent, lymphocytes—21 per cent and monocytes—5 per cent.

In June 1945 eosinophilia was 35 per cent. On 22-7-45 blood film report gives the following differential count of W.B.C.'s:—

Polymorphonuclears—69 per cent, eosinophils—14 per cent, lymphocytes—15 per cent and monocytes—2 per cent.

X-ray findings—His x-ray report of lungs on 31-3-45 shows general mottlings in both lungs with marked striations. In June '45 screening report by the radiologist says both lungs clear.

On 31-7-45 when I examined him I found his lungs quite normal. His weight was 128 lbs. He regained his normal colour and looked quite healthy.

Discussion

Whether this eosinophilia with its lung complications is a disease entity or not has been debated. I consider it as a distinct disease by itself and name it eosinophilic pseudo-leukæmia. This term will include two clinical conditions *i.e.*, eosinophilia with lung infiltration and eosinophilia with splenomegaly. On reading both diseases together I find both have the same pathological condition in blood attended in one case with lung phenomenon and in the other with splenic enlargement. In leukæmia presence of immature cells in blood circulation is just as important as the type of cell. Absence of immature cells in general circulation (or if at all found they are few and far between) is a marked feature in eosinophilic lung and hence pseudo-leukæmia is a proper word for its nomenclature. Eosinophilia of such a high percentage is never seen in any other known disease. That the disease breeds true to one particular type of white blood cell is really a very strong argument in favour of considering it an entity by itself.

It should be distinctly differentiated from asthma. It is not a variety of asthma as some people think it to be. There are really no asthma-like symptoms in this disease. It is not accompanied with sudden spasms of dyspnœa. Patients complain of spasmodic hacking cough. Low fever and emaciation which is the usual accompaniment of eosinophilic lung is not met with in asthma. Amongst 175 patients of eosinophilic lung reported by Frimodt-Moller and Barton only 35 complained of asthma and bronchitis, while 153 complained of cough, 144 of fever and 117 of loss of weight and strength. Eosinophilia in asthma never reaches to such a high degree as in this disease. And lastly in eosinophilic pseudo-leukæmia eosinophilia of high degree is sustained and prolonged for months till it is relieved by a specific treatment.

In my considered opinion it cannot be called an allergic pneumonia. If eosinophilia is present in allergic condition it can also be a concomitant symptom in other diseases. Besides this we do not possess sufficient postmortem material to find out the actual pathological and histological changes in eosinophilic lung. Presence of other allergic symptoms is not an essential and constant feature of this lung. My patient did not show allergic symptoms to any drugs or food. 48 of Maire's 100 cases have not presented other allergic manifestations. In allergy total white cell count is not raised and eosinophilia is generally never more than 20 per cent. Infiltration of lungs in the disease under discussion is only a part of the picture. We do not call enlarged spleen in eosinophilic leukæmia with splenomegaly as an allergic splenomegaly.

In ascaris infection syndrome is short and fleeting. It cannot prolong into an illness of months and one ought to find some larvæ in the sputum which does not happen in this disease.

Another very important laboratory finding makes me believe it to be an independent disease. Wassermann blood test is positive in many cases and becomes negative when eosinophilia goes down (Greval, 1940 and Gupta, 1945) Kahn is always negative unless the patient is concurrently suffering from syphilis. Positive Wassermann is a strong point to suggest the possibility of bacterial origin. On account of this positive reaction Greval has suggested the name of lecithinophilic eosinophilia.

The aetiological factor is probably an undetected virus which gives rise to a chronic but benign syndrome in which either lung or spleen bears the brunt of the disease. The virus is susceptible to neo-arsphenamine which can be clearly seen in the definite improvement of the patient's condition. It acts on the myeloid tissue by a slow process which gives sufficient time for precursors of eosinophils to mature fully before they enter general circulation. When the virus is rendered feeble and innocuous by arsenic treatment neutrophils begin to appear in circulation keeping down the number of eosinophils. As long as the virus is active the typical picture of the disease is maintained which is clearly seen in eosinophilia without immature cells.

Lœffler's syndrome is in my opinion a manifestation of eosinophilic pseudo-leukæmia in its short but active form. It lasts for a few days only and clears up without any specific treatment. The virus is probably overcome by the defensive forces of the body and so the typical condition does not last long. Can Lœffller's syndrome be a primary infection which later on relapses into a chronic manifestation of eosinophilic lung?

What percentage should constitute an abnormal eosinophilia? European workers take 7 to 8 per cent as abnormal. Wright in his Applied Physiology gives 1 to 4 per cent as a normal figure and 150 to 400 per c.mm. as an absolute normal count. Frimodt-Moller and Barton have chosen 20 per cent for their investigation. Their argument for selecting this figure is that typical x-ray findings were not to be seen below this figure. My patient showed complete improvement and good health in spite of 14 per cent eosinophilia. It would thus appear that count above 20 per cent should raise our suspicion about this disease and a total white cell count should be done to find out leucocytosis. In this way we may diagnose early cases of eosinophilic lung and give them proper treatment. Importance of blood and sputum examination, of x-ray findings and careful clinical examination cannot be over-estimated in cases with low fever, cough and enlarged spleen before they are diagnosed as tuberculosis or chronic malaria in the tropics.

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SULPHONAMIDES IN OPHTHALMIC PRACTICE

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The addition of sulphonamide compounds to chemotherapy is probably the greatest advance in medical science for many years. These drugs have been already tried in the treatment of many inflammatory diseases with marked success. In ophthalmic practice, they have been proved especially effective in the treatment of conjunctivitis particularly the gonococcal conjunctivitis, trachoma, corneal ulcers and for preventing and for controlling infections after intraocular operations.

During the past several years, several sulfanilamide compounds have been prepared. Three of these compounds sulfanilamide, sulfapyridine and sulfathiazole produce full therapeutic effects attainable by any of the drugs in this group. Experience gained by the use of these drugs in eye practice is recorded here.

In this paper I desire to draw the attention of my fellow ophthalmologists to a method of treatment, the efficacy of which one can prove himself easily. With the results that we get and from the simplicity of the treatment I am led to believe that from now on, it will be possible for a practitioner to treat terrible eye diseases that are capable of destroying the entire globe like gonorrheal conjunctivitis, trachoma, and severe corneal ulcers and post-operative infections effectively with drugs that will always be at hand and the application of which is extremely simple and free from pain of any nature.

In ophthalmology however, a consensus of opinion is developing with regard to local treatment in the form of concentrated solutions, ointments and powders having a definite curative effect in a number of infections of conjunctiva and cornea. The sulfapyridine used locally is very effective in preventing as well as curing eye infections. This is explained by the fact that while systemic administration of sulphonamides, one aims to produce concentrations of 6 or 7 mg. per 100 c.c. in the blood and tissues, the local implantation produces much higher concentrations in the affected area and the maintenance of these concentrations over longer period.

Loe has shown that when powder is used, the concentrations in the aqueous was found to be considerably higher than blood without any untoward results. Thus the local insufflation of sulfapyridine appears to be a highly efficient method of preventing and combating infections in eye affections. The common toxic manifestations like general malaise or vomiting were not observed when this drug was used locally alone. The most important point to be remembered is that, it should be administered sufficiently often, every four hours, to maintain an adequate concentration at the site of infection. It should not be less than four times a day. The essential idea was to expose the organisms situated in the conjunctival sac directly to the drug. Why should we use the drug in solution, when we know that the tears, which consist of warm salt solution could very well dissolve the drug placed in powder form on the inner surface of the lids? With a spatula a certain quantity of powder should be

deposited on the cornea and in the fornices under the lids. The patients state that they feel no irritation. This should be ordered to be done every four hours after washing the eye with a solution of boric lotion or weak mercury lotion.

As the eye affections are mostly caused by pneumococcal, staphylococcal and gonococcal infections, sulfapyridine is more effective in these conditions than sulfanilamide. It should be the drug of choice for local use. This drug is also effective in hæmolytic streptococcal infections, though it may not be superior to sulfanilamide in this affection. Like sulfanilamide, the action of sulfapyridine is bacteriostatic on the organisms, allowing body immunity to overcome the infection. In contrast to sulfanilamide, there is evidence to show that sulfapyridine seems to exert a definite bactericidal as well as bacteriostatic effect on most types of organisms.

In serious cases sulfonamides were given internally also to curtail the period of treatment. With slight modifications the treatment recommended by Loe was adopted for the large majority of patients. Loe's method consists of oral administration of sulfanilamide gr. 1/3 per pound of body weight for the first ten days treatment with the reduction of ¼ gr. for the following 14 days. In my cases for the first two or three years sulfanilamide was used internally and since last two or three years sulfathiazole in the form of cibazol was used, as the latter drug was found to be much softer producing no toxic symptoms of any nature and giving better results. In severe cases 2 tablets were given three or four times a day according to requirements for the first 3 or 4 days during which time symptoms abated and the patient showed definite improvements. Then four tablets per day, one every four hours were given for 3 or 4 weeks according to severity of the case. In some cases of long-standing trachoma it had to be extended to six weeks without any harm to the patient. As comparatively lower doses were used internally no serious toxic symptoms of any nature were observed in any case. Some patients did not like the drug and felt uncomfortable with it, so in those cases internal administration was given up and only sulfapyridine was used locally.

I shall only take up those conditions in which the action of sulfonamides is definite and clear.

Muco-purulent conjunctivitis—If insufflations with sulfapyridine is used in conjunctivitis, the redness and discharge disappear in 2 or 3 days time. The effects are as good as silver salts and in some cases even better.

Gonococcal conjunctivitis—Sulfonamides are now used as a routine procedure in all clinics for gonococcal conjunctivitis. With adequate chemotherapy nearly all eye patients with gonococcal conjunctivitis exhibit a clinical and bacteriological cure within 3 or 4 days. However it is now known that sulfapyridine is more effective than sulfanilamide against all strains of gonococci and recent evidence indicates that sulfathiazole is even more effective than sulfapyridine.

Pseudomembranous conjunctivitis—The oral administration of small doses of sulfanilamide or sulfathiazole together with local use of sulfapyridine is effective in curing streptococcal pseudomembranous conjunctivitis. Signs of clinical improvement are evident after 2 or 3 days treatment. The cure is complete within eight or nine days.

Trachoma—The trachoma is so prevalent in India that its treatment should receive our first consideration. While the local application of metallic silver salts (silver or copper) have long been established as perhaps the most reliable of the choices available, they nevertheless have limitations, since such treatments are prolonged, painful and scar producing, and their end-results are uncertain, as the frequent recurrences are common. The introduction of sulfanilamide and its derivatives have revolutionized the treatment for trachoma. The marked success achieved with these prove the usefulness of these drugs in trachoma. With the change of treatment, the prognosis is also changed. What we could not achieve for months, now we are able to handle serious cases with marked success in a few weeks time, as you will see from the cases reported. Subjective symptoms such as pain, photophobia and lacrymation disappear in forty eight hours and the pannus and infiltration of the cornea absorb to a great extent in eight days. The healing continues from week to week till clinical recovery takes place in three to six weeks time according to the severity of the case. Secondary infections with Weeks bacillus, diplobacilli of Morax, pneumococci, and gonococci are controlled in a few days time. In general terms, it may be said that the effects of sulfonamide therapy in trachoma are most dramatic in those cases in which the disease has produced serious clinical manifestations, whereas in subclinical trachoma, in which the vision is unaffected, in which the patient has no serious subjective symptoms, sulfonamides appear to have less dramatic effect. However mild cases can be cured easily by local treatment alone. In some cases follicles do not disappear readily. In such cases grattage or expression should be done.

The following cases will show the efficacy of this treatment.

1. Mr. J., 20 years old, consulted me on 6th October. He had marked trachoma with hypertrophied, red and congested conjunctiva, pannus and several corneal ulcers in both the eyes. He was treated by his last doctor for about 20 days with silver salts and atropine. As his clinical condition did not get better under the treatment, and his pain considerably increased, so that he could not get sleep for some days, he came under my treatment. He was admitted to the Hospital, atropine and sulfapyridine used locally. Insufflation of the powder every four hours was instituted. Sulfathiazole *i.e.*, cibazol was given internally two tablets four times every four hours for first two days. Then 3 times for another four days. After one week one tablet every four hours was given. Pain and watering got less after 2 days treatment. Ulcers healed and the patient was discharged in six weeks time. His vision from F.M. at the time of admission came to 6/60 at the time of discharge.

2. Mrs. J., 20 years old, consulted me on 4th October. She had trachoma of several years standing and had relapses off and on. Her last attack started two months back. In these two months, she changed four doctors as her clinical symptoms and the severe

pain that she felt did not get better with the usual treatment. The pain was so severe that she did not get any sleep and her last doctor had to give her morphine injections. When I saw her on 4th October her palpebral conjunctiva in left eye was hypertrophied, red and congested. She had pannus and central fairly large corneal ulcer. She was admitted to Hospital and put on usual atropine, sulfapyridine insufflations every four hours locally, and sulfathiazole internally. Her pain subsided after 3 or 4 days treatment. Ulcer healed and she was discharged from hospital on 28th October *i.e.*, 24 days after admission.

3. Mr. J. consulted me on 16th July 1944. He had chronic trachoma and used to get off and on attacks since last 5 or 6 years. His last attack started two months back. He got a little better with the usual treatment adopted by his doctor and resumed work, but again he got relapse one month back. During this one month he was treated by his doctor with the usual cauterizations with tinc. iodine, carbolic acid, and thermocautery, argyrol, atropine and noviform ointment were also used. With this treatment, ulcer instead of healing went on progressing and he felt a good deal of pain. When he consulted me he had sloughing ulcer and the whole of the cornea was more or less ulcerated. He was admitted to the Hospital and put on atropine, sulfapyridine insufflations every 4 hours and sulfathiazole internally. Next day the pain and watering were less, the progress of the ulcer stopped. Day by day the ulcer went on healing under the treatment till the ulcer completely healed and he was discharged on 24th July *i.e.*, 14 days after his admission to the hospital.

Corneal Ulcers—Almost all corneal ulcers heal under the treatment of atropine and local sulfapyridine insufflations four hourly and sulfathiazole internally. This treatment is particularly indicated in hypopyon ulcers. This affection is mostly caused by pneumococci and sulfapyridine works specifically in this condition. One patient consulted me for hypopyon ulcer and I used atropine and sulfapyridine powder insufflations at 2 o'clock and the eye was bandaged. At 6 o'clock when I removed the bandage for further insufflations, the hypopyon was half gone and the next day it disappeared completely. A child of one year was brought to me for the suppuration of the cornea. With three days sulfapyridine treatment progress of the suppuration stopped and healing started.

Phlyctenular ulcers also yield easily to this line of treatment. But if some preparation of cod liver oil and calcium are given the cure is more rapid and more permanent.

A child of 2 years was brought to me with marked phlyctenular ulcers in both the eyes. With this one week's treatment the ulcers healed up. A child of 5 years was brought to me with fascicular ulcer. With this treatment healing was brought about in a week's time without cauterizations.

The healing with sulfapyridine is so definite and certain that you are not required to cauterize the ulcers either with carbolic acid or actual cautery. In 1935 I had occasions to cauterize the septic ulcers 17 times. In 1936—16 times, 1937—11 times, 1938—7 times, 1939—6 times and 1940—5 times. Now hardly once or twice I am required to use these cauterizations for progressive ulcers. This year I had only once used cautery and that too for a case that was healing well under sulfapyridine treatment, but the central hard slough would not be absorbed readily, so I burnt away that hard stuff with cautery, and the healing completed readily. The requirements and use of cyanide of mercury injections are considerably reduced. On the contrary if the milk injections are used with the above line of treatment the cure is more rapid.

Infections of unknown etiology—Frequently especially intraocular infections it is not possible to determine the cause of the infection in the eye or orbit. In any such cases the best drugs to use is sulfapyridine locally and sulfathiazole internally. Often times you will get good results from this treatment.

Post-operative infections—In post-operative infections these drugs are able to save the eye, if used at a very early stage.

If some time is allowed to pass they may not be able to save the eyes. Sometimes we get operated cases, who complain of pain, watering and photophobia persisting good many days after the cataract operation. In such cases, on examination we find that the incision scar looks grey and bigger, the upper part of cornea is hazy, there is slight ciliary injection and mild iritis. In such cases of mild infection I have been able to get good results with this line of treatment. In some cases of mild post-operative infections soluseptasine was injected under the conjunctiva about ½ to 1 c.c. and the method gave good results.

Prophylatic use—In the past too much attention has been paid to the curative side of these drugs, better results might be expected if workers take advantage of its bacteriostatic action and use prophylactically before surgical interventions. This bacteriostatic action of sulfonamides is accepted by almost all workers. It is quite reasonable that these drugs should be administered internally before operations and used immediately after operations, so that infections may not take place. A very weak concentration will completely inhibit the growth of small number of sensitive bacteria, whereas a very large implant will grow out in a higher concentration that can be attained in the body. Clinical and experimental workers have confirmed the fact that the prophylatic introduction of sulfonamides before closing compound fractures brings about a significant decrease in resulting infections without delaying the healing of bones and soft tissues. Similarly, if before cataract operations we give cibazol internally and insufflate sulfapyridine powder after the operations are completed, and use it as insufflations in subsequent dressings, not only we do not get septic infections, but even mild iritis is rare, even if you have left cortex at the time of operation. Ciliary injection is comparatively much less, wound heals, a.c. forms faster and cornea remains clear. The same thing applies to other intraoccular operations.

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EXPERIENCE ON FOOD RATIONING

The history of food rationing in India is peculiar. One saw food rationing on a wide scale being introduced in England almost simultaneously with the declaration of War. Germany started it long before on a basis of self sufficiency. India although officially was in a state of war with Germany, still lagged behind on question of food. Even the threat of Japan in the East could not stimulate the Government of India to think of food. India was still an unknown factor on the question of food with the Government, even with its hungry 400 million. In spite of this India was tapped for food wherever and whenever there was a deficit on any plea that seemed suitable for the occasion. According to a statement issued by the Government of India the total export of food grains from India during 1942-1943 was 370,000 tons. During the period before war, economists, nutritionists, statisticians were repeatedly pointing out about the danger of increasing population and dwindling food production. Nothing was done to improve the food position. A portfolio of food was not created. There was no plan, no organisation, not even serious deliberation about the agricultural problem. There was no plan to improve the manure, reclamation of cultivable waste lands, scientific methods of agriculture. Government launched a "Grow more food" campaign in the lobbies, restaurants, over the radio and in the kitchen gardens. It blamed the increasing population of India and loss of imports from Burma as soon as Japan marched on Burma in 1942. As pointed out above exports from India still continued with the inevitable onset of famine in Bengal, during the latter part of 1943. Famine took away 1·5 million dead in the province of Bengal alone, and Government of India started a sort of stop-gap food rationing. As there was no All-India plan of food distribution, prices of food materials soared high, black-market extended, interprovincial smuggling of rice and wheat increased to an unimaginable extent and bribery, corruption and nepotism thrived all over. Men made money over the skeletons of the people of the land and Government looked helpless.

One realises the difficulty of starting food rationing overnight. But that argument is not tenable when one knows definitely that the food position of our country was unsatisfactory in peace time. How could England start food rationing within three days of the declaration of War and distribute about 50 million ration cards? Was it impossible to do the same thing in all the big cities and industrial towns in one month after the declaration of War in September 1939? The population involved could not be more than the whole of British Isles. This would have stopped the soaring prices, black market and much of corruption. Government of India started a method of 'Price Control' with a string of "Control Shops" here and there. There was no control over 'Control Shops' or their owners, who used to refuse almost half the people in the queue and black market flourished. Scientific food rationing was started in Bombay, followed by Madras and other provinces. In Bengal it was introduced towards the early part of 1944 after the famine. After a period of 2 years, food rationing could not be introduced, in all the provincial towns. Now every province has got a mixture of food rationing and price control. It is estimated that 57 million of a total population of 400 million are subject to rationing regulations. The most successful of rationing schemes are operating in areas of Bombay, Mysore and Travancore. It must be clearly understood that by food rationing in India is meant rationing of only rice, wheat, salt and sugar. It is altogether unlike rationing in England where meat, milk, fish, eggs, fats, sugar and fruits are included. There total number of calories for each person and increase in the nutritive value in 'our loaf' form subjects of serious discussion among scientists and in the Parliament. Protein, fat, carbohydrate, mineral salts and vitamins are evenly distributed so as to ensure health and morale. Attention is also given so as not to make diet much plainer and less attractive.

The only benefit of rationing in India is that rice, wheat and sugar are now available at a certain price. It has subdued black market in the above commodities to some extent. But this piece-meal rationing here and there has many drawbacks. When through rationing the basic needs of food were available in towns, there was up rush of people from the rural to the urban area. On the contrary at present prices are higher in the rationed than in the non-rationed area, so there is a great deal of smuggling of rice and wheat from the non-rationed to rationed area. Two things are deplorable in the rationed area. Firstly, the quality of rice and wheat is not uniform and at times they are inedible. Secondly, the tendency of price of the above commodities is upwards. This is because of the very top-heavy administration and almost criminal waste of food stuffs due to lack of knowledge in storing them properly. Rationing has failed to reduce the price of food. In January 1945 the all-India index of wholesale price of food articles (base last week of August 1939—100) worked out to 235·6. The following table indicates the percentage of increase of some essential food products.

Article	*January 1940*	*January 1945*	*Percentage of increase*
Cereals—			
Rice	Rs. A. P.	Rs. A. P.	
Fine ..	5 8 0 md.	16 4 0 md.	295%
Medium ..	4 8 0 „	..	..
Coarse ..	3 12 0 „	..	..
Atta ..	5 0 0 „	12 8 0 „	250%
Bread ..	0 3 0 lb.	0 5 0 lb.	166%
Dal			
Chola (Gram)	3 0 0 md.	15 0 0 md.	500%
Arhar ..	5 0 0 „	25 0 0 „	500%
Vegetables			
Potato ..	0 1 0 sr.	0 6 0 sr.	600%
Meat			
Mutton ..	1 4 0 „	3 0 0 „	238%

Fish					
Rohit & Katla	1 4 0 „	2 8 0 „	200%
Mustard Oil ..	14 0 0 md.	47 8 0 md.	339%
Egg ..	2 for 1 anna	0 2 0 each	400%
Milk ..	5 srs. per rupee	2½ srs. per rupee	200%
Butter			
Cow's ..	1 4 0 sr.	5 0 0 sr.	400%

The prices have fluctuated little from January 1945 to January 1946. Great Britain not withstanding her dependence on imports of foodstuffs, is able to keep prices regulated at 27 per cent above pre-war prices while raising average income by 30 per cent. The fact that India suffers from an unregulated rise in cost and a fractional rise in wage earners' income, is an unanswerable indictment on the whole Government, specially its Department of Civil Supplies. High prices and low vitality go together. Because the diet of the people has gone from bad to worse regarding the nutritive value, protein, fat and carbohydrate are disproportionately distributed. In the majority, protein and fat are dropped to save expenses. By the introduction of food rationing the Government took a great responsibility. It has still a good opportunity of educating the people as regards scientific dieting and thus make rationing a success. The Government should remember also that there is the danger of being a direct party responsible for enhancing the slow process of malnutrition of India's millions.

The whole picture has lately been overshadowed by the spectre of impending famine. Mr. B. R. Sen, Food Secretary, opening the food debate in the Central Assembly on January 30, 1946, described the serious food situation in the country and said that this year "we have had a devastating cyclone, a failure of north-east monsoon in Southern India and now the threat of a failure of winter rain in U. P. and North Western India". The worse hit sections are the southern parts of Bombay province and Malawar, on the West Coast of India, Central and Eastern Coastal areas of Madras, and Mysore and Travancore States in the Central and Southern sections of the Peninsula. Lack of accurate statistics hampers the Government in its effort to make an exact estimate of the needs, but unofficial figures indicated that the shortage of rice might come to as much as four million tons. Much earlier, foreign writers[1] drew attention to an impending World Famine. It was estimated that both India and China are each 2 million tons short in their supplies of rice and other grains. Continental Europe will require about 12 million tons of bread grain.

It is apprehended that famine in India of a scope surpassing the Bengal disaster of 1943 may have to be tackled in near future. As a means of meeting the problem the Government is planning a unified procurement programme and also tightening up the present scale of rationing. But these are all temporary measures. The Government has put forward the usual excuse for this situation. They are shipping shortage preventing imports, annual increase of 5 million in Indian population, failure of the monsoon in parts of India. These are not new factors in food problem of India. They are as old as India herself. Has the Government of India got to be reminded again of a report made 20 years ago by the Royal Commission of Agriculture in India? If 50 per cent of the recommendations of that report had been put into effect, India would not have found herself in the present situation. What was the Government doing during these 20 years?

[1] EDITORIAL—*Lancet II*, 565, 1945.

(*Continued from page 153*)

SUMMARY

With regard to the results of this treatment of sulfapyridine locally and sulfathiazole internally, following observations could be made.

1. That this is the recognised method of treatment for gonococcal conjunctivitis, and the cure is more or less definite in a few days time.

2. That in trachoma this treatment is a great advance over the usual method, as it curtails time, is painless and the chances of relapses are much less, and the surgical interventions are not required.

3. That all corneal ulcers heal away under this treatment without cauterizations therefore the resulting scar is much thinner and fainter and the vision better.

4. That the prophylactic use of these drugs in intraocular operations prevent infections. In cases of infections, if these drugs are pushed at a very early stage, the infections could be controlled in good many cases.

CURRENT MEDICAL LITERATURE

Erythema Nodosum and Tuberculosis

Gray (*Brit. M. J.*, **2**:286, 1945) gives in the following lines the summary of his observations:—

Nine cases of erythema nodosum are described. Seven were of school age; two were young adults. Six are males, three are females. Three are contacts of known cases of pulmonary tuberculosis, and another has a family history of tuberculosis. Two have been visitors to a tuberculous household, and two more have relatives suffering from chronic cough who refuse to be examined. Only two gave no history of suspicious contact. All the children gave a positive tuberculin reaction. The tuberculous lesions met with were pleural effusion, pulmonary tuberculosis, phlyctenular conjunctivitis with corneal ulcers, tuberculous cervical glands, enlarged or calcified hilar glands, and a simple primary complex. No history of rheumatism was given by any of the patients.

Erythema nodosum is often associated with tuberculous lesion, and is a manifestation of tuberculous infection. All cases should be referred to the tuberculosis officer for investigation and follow-up. Every case of erythema nodosum should be regarded as a newly infected case of tuberculosis, and therefore search should be made among family and friends for the unknown source of infection. While the cases may develop nothing serious, the occurrence of ill-health and minor tuberculous lesions is frequent enough to warrant attendance at a tuberculosis dispensary in every case.

Chronic Hypochloraemia Simulating Psychneurosis

Saphir (*J.A.M.A.*, **129**:510, 1945) reports 10 cases of chronic hypochloræmia and writes that an analysis of these cases reveals that chronic hypochloræmia can give rise to a variety of symptoms. These symptoms may be divided into two groups, one related to the intestinal tract, the other to the nervous system. Intestinal symptoms were vague epigastric distress without definite relation to food intake, abdominal cramps, anorexia, frequent nausea and occasional vomiting. Symptoms related to the nervous system were headaches, dizziness, tremor, hyperreflexia, hyperhidrosis, nervousness, apprehension, restlessness, insomnia with loss of pep and strength, depression, personality changes and even frank anxiety.

Consequently all the patients were originally assumed to be suffering from a psychoneurosis. For even when the alimentary symptoms predominated, the absence of significant organic and laboratory findings led the author to suspect the presence of a conversion psychoneurosis with psychosomatic manifestations of the intestinal tract.

It was only through determination of the blood chlorides that the true nature of the disorder became manifest. Rapid improvement of all 'psychoneurotic' symptoms took place on restoration of the blood chloride level to normal.

Just what factors were responsible for the salt deficiency in these cases is not clear. It may be reasoned that the patients had taken enough salt to prevent a sudden depletion of chloride stores with its typical picture of acute heat exhaustion. But they had not taken enough to prevent a gradually increasing chloride deficit. The history obtained from these patients appears to substantiate this assumption.

Dietary Accommodation in Renal Failure

The composition of the blood is determined not by what the mouth ingests but by what the kidneys hold back. When critical selection is seriously reduced by disease the kidneys keep what they should excrete, and eventually there is uræmia. On an ordinary mixed diet the end-products excreted by the kidneys are predominantly acid and the protein end-products demand much renal work. In renal failure, therefore, it is reasonable to suppose that a diet which provides an alkaline ash and fewer protein end-products lessens renal work. The dietary coat can be cut according to the renal cloth, and there may then be an increased prospect of the kidneys' living within their diminshed exercise tolerance. A diet conforming to these principles has been advocated by Kempner (*North Carolina M. J.*, **6**:61, 1945). Although, perhaps, he arrives at his working hypothesis in a more original manner, Kempner reports good results in the treatment of renal disease with a diet composed of rice and fruit juices. In a daily total of 2,000 calories the diet contains only 20 gm. of protein and 5 gm. fat. Unless there is evidence of salt deprivation, no salt is allowed. No extra water is given, and the total fluid is usually limited to 700-1,000 c.cm. of fruit juices. A vitamin and iron supplement is given daily. Nitrogen equilibrium was maintained on the diet over prolonged periods, and there was no significant depletion of salt or fall in hæmoglobin. Such a diet would be unobtainable in England at the present time, and Kempner agreed it will never be popular. The food is monotonous and does not taste good. The patient has to eat it for a long time before its full effects become apparent, and the diet becomes worthless if it is modified by so-called small or minimal additions according to the patient's own taste. There is, in fact, only one excuse for such a therapy, and that is, it helps. The most impressive effects of Kempner's diet were in chronic Bright's diesase with renal failure. In more than half the cases treated there were a reduction of retained nitrogenous end-products, a fall in blood pressure, and a general clinical improvement. In essesential hypertension, also, the blood pressure was often significantly reduced. The results are reminder that even when structural and functional contraction of the kidneys is beyond repair, what the mouth ingests may rectify what the kidneys keep. It would perhaps embarrass the kidneys less in the process if they were provided with a more generous fluid intake.—*Brit. M. J.*, **2**:696, 1945.

Jaundice Therapy of Rheumatoid Arthritis

Gardner and others (*Brit. M. J.*, **2**:677, 1945) writes that jaundice was induced in 32 patients with rheumatoid arthritis, and temporary improvement in the latter condition was obtained in 25 cases.

The remissions were unequal in degree and of short duration. Ten patients became completely free from pain and swelling, and 15 showed some improvement. The average period during which optimal improvement was observed was 42 days, but a longer time elapsed before the joints reverted to their pre-icteric condition.

Complete freedom from pain and swelling was obtained more often in patients who had had rheumatoid arthritis for less than 5 years than in those who had it for more than 5 years.

There was no definite relationship between the intensity of the jaundice and the type of remission evoked.

In many cases a fall in the E.S.R. was noticed during the icteric phase. This was followed by a rise to a level above that recorded before jaundice was induced. These changes did not necessarily correspond to changes in the joint condition. A similar phenomenon has been observed when patients with active tuberculosis develop infective hepatitis.

Caffeine and Peptic Ulcer

Allard (*Dtsch. Arch. Klin. Med.*, **80**:510, 1940) observed the production of acute gastric erosion and hæmorrhage, in man and dog, after the ingestion of synthetic theophylline, and numerous later workers have confirmed that drugs of the caffeine series, administered orally or by injection, may induce acute gastric erosion within a few hours. Roth and Ivy (*Am. J. Physiol.*, **141**:454, 1944) who have shown previously that the development of the caffeine-induced ulcer is associated with increased secretion of acid and pepsin, and that it can be accelerated by alternate administration of caffeine and histamine, have now (*Surgery*, **17**:644, 1945) studied sections of the gastric mucosa of the cat excised serially by a special technique at intervals of 15 minutes after the slow intravenous injection of 250 mg. caffeine sodium benzoate. They describe a regular sequence of changes in the mucosa: vasodilatation and engorgement followed by vascular stasis, local anoxia, increased capillary permeability, transudation, extravasation of blood elements, and proceeding finally to decreased cell nutrition. Roth and Ivy are accordingly of the opinion that the acute caffeine-induced ulcers arise by the digestive effect exercised by pepsin and hydrochloric acid, formed in excess, upon a gastric mucosa specifically devitalized by circulating caffeine. They add that the pharmacodynamic action of caffeine upon the stomach may or may not be partly or wholly dependent upon its excitatory action on the central nervous system.

Merendino and his fellow-workers (*Surgery*, **17**:650, 1945) have examined the effect of daily intramuscular injection of caffeine alkaloid in a besswax medium in guinea-pigs and cats. Four out of 10 guinea-pigs and 11 out of 26 cats developed typical punched-out ulcers. In dogs with prepared gastric pouches it was shown that the subcutaneous injection of 1,200 mg. of aqueous caffeine alkaloid, or the daily intramuscular injection of 2,500 mg. of caffeine alkaloid in beeswax, increased the volume and acidity of gastric secretion. This effect persisted even after division of the vagus, and is presumed to be due to the direct action of caffeine upon the gastric mucosa. This expereimental work is not without direct and immediate application to man. Merendino has verified that two cupfuls of coffee taken by mouth or by stomach tube increase the volume and acidity of gastric secretion, and that the increase is most dramatic if the coffee is drunk cold and black. Judd (*Bull. Am. College Surg.*, **28**:46, 1943) in 1942 reported the perforation of a peptic ulcer in a young man, with no previous experience of dyspepsia, after the ingestion of 150 bottles of cocacola during a five-day heat-wave. Another patient, whose duodenal ulcer proved highly resistant to treatment, proved to be a cocacola addict. The relation of peptic ulcer to caffeine in these two clinical examples may not be entirely causal, but the experimental work brought together in the papers cited is at least an adequate justification for eliminating caffeine-containing beverages from the diet of ulcer patients.—*Brit. M. J.*, **2**:505, 1945.

Late Secondary Tonsillar Hemorrhage

Neivert (*Arch. Otolaryngol*, **42**:14, 1945) writes that tonsillectomy and adenoidectomy are not infrequently complicated by secondary hæmorrhage occurring generally on the sixth or the seventh day. The author learnt that in Europe these secondary hæmorrhages are much less frequent and the difference that seemed significant was that acetylsalicylic acid is extensively prescribed in this country as it also is in Canada and England, whereas in Central Europe amidopyrine is the drug of choice. Workers in the department of biochemistry of the Wisconsin Agricultural Experiment Station showed that salicylic acid and sodium salicylate induced hypoprothrombinæmia in rats kept on a ration low in vitamin K. The animals could be protected against this action of salicylic acid by administration of a vitamin K preparation. Estimations of prothrombin time done on a large number of patients at the author's hospital revealed that in some subjects a daily dose of 2·4 gm. of acetylsalicylic acid will produce an elevation in prothrombin time on the next day, whereas in others it will be much longer before a significant rise will be discernible but such a rise will occur eventually. These studies afford corroborative evidence that administration of salicylates reseults in hypoprothrombinæmia. In view of the fact that acetylsalicylic acid, by virtue of its effectiveness and its comparative nontoxicity, is the most widely used analgesic, the author thought it advisable, rather than to eliminate it, to combine it with an agent which will counteract its effect on prothrombin. The water soluble vitamin K-like compound synkayvite (tetrasodium 2-methyl-l, 4 naphthohydroquinone diphosphoric acid ester) prevents this undesirable side effect of acetylsalicylic acid. The combined acetylsalicylic acid and synkayvite medication was tried on a broader scale. Only 4 among 283 patients were troubled by late tonsillar bleeding. This author concludes that while in rare cases the cause of late post-tonsillectomy hæmorrhage may be trauma, mentsruation, infection, deficiency of vitamin C or some blood dyscrasia, observations suggest that one of the most important factors is a reduction in the prothrombin of the blood brought about by the use of acetylsalicylic acid or salicylates.

Abuse of Prolonged Rest in the Aged

Norman (*Minnesota Med.*, **28**:803, 1945) writes that prolonged bed rest may add to the risk in any illness of the aged who are already handicapped and many cardiovascular patients do better if out of bed early. Wound healing is more rapid with early rising after operation and wounds have fewer early or late ruptures; motion favours healing. There will be fewer pulmonary complications, and vascular accidents are markedly reduced.

In old people the use of urinal and bedpan is dreaded and early rising permits them to go to the toilet. Distention is lessened and urinary complications less frequent. The old patient is very happy to be up and feels that there is hope for his ultimate recovery. Early rising should mean early walking. Patients do not dread hospitalization if they know that they will not be kept in bed long.

The principle of little bed rest for the old patient should be adhered to in the patient who comes in for pre-operative conditioning. Such patient should be up and around as much as possible, have a proper diet and be out of doors if possible, even though it be by wheel chair.

Boric Acid Ointment

Peiffer and others (*J.A.M.A.*, **128**:266, 1945) from a study of possible intoxication in the treatment of burns give in the following lines the summary of their observations:—

1. Boric acid is absorbed in toxic quantities from ointments applied to burned areas or to wounds involving loss or damage to large areas of skin.

2. When a 5 per cent boric acid solution is used to irrigate cavities most of the boric acid is absorbed by the tissues.

3. While boric acid is not toxic when administered in a single large dose, repeated doses result in accumulation in the brain, liver and body fat.

4. The boron occurs in both the white matter and grey matter of all parts of the central nervous system and in the peripheral nerves. The spinal cord and grey matter of the cerebrum contain the highest amounts.

5. The liver is only slightly affected histologically by chronic poisoning. The kidney shows tubular degeneration, while the brain and spinal cord show neuronophagia and hyperchromatosis. The skin shows polymorphonuclear infiltration and vascular engorgement.

6. As little as one third the median lethal dose, or treatment of a burn involving only 4 per cent of the surface area of the body with U.S.P. 10 per cent ointment, will produce pathologic changes in the central nervous system.

7. When repeated daily doses as small as 200 mg. per kilogram are given subcutaneously, fourteen to eighteen days are required before urinary excretion reached a plateau. This, together with the fact that boric acid can still be found in the brain of animals four days after discontinuation of series of doses, indicates cumulative action.

8. The growth of immature rats is not influenced by 0·1 per cent of boric acid in the drinking water, but a level of 0·25 per cent retards normal growth after twenty days.

9. The data do not provide any evidence of a depressant action of boric acid on the blood forming organs.

10. A definite increase in urinary phosphorus excretion occurs after intravenous doses of boric acid.

11. The boron found in the brain is not combined with phospholipid or cholesterol but is probably present in some simple combination with glycerol or other polyhydroxyl compounds.

12. Death is due to a shocklike syndrome when large doses are given. If moderate dosage is given over a period of several days death may result from inaction due to convulsive tremors and meningismus. When intravenous fluids are given to prevent early deaths, some animals develop anuria at 2·5 times the untreated median lethal dose.

13. Polyhydroxyl organic compounds such as mannitol, glucose or glycerol are not antidotal to boric acid. Large intravenous doses of isotonic solution of three chlorides and plasma definitely antidote the toxicity.

In conclusion the authors write that boric acid, whether applied in the form of an ointment or a saturated solution to extensive wounds, is a cumulative poison. The weak antiseptic value of boric acid suggests that for medicinal use other more active and less potentially harmful therapeutic agent should be employed.

Clinical Effects of the Local Use of Sulphonamides on the Eyes

Alvaro (*Am. J. Ophthalmol.*, **28**:497, 1945) writes that the fact that the sulphonamides are almost innocuous to the ocular tissues when applied locally, their easy penetration when thus applied, the almost complete absence of symptoms of intolerance to this kind of sulphonamide therapy, and the great effectiveness with which the drug acts in several eye diseases make it probable that the topical use of sulphonamides will largely supplant their oral administration.

Sulphanilamide, sulphathiazole, sulphadiazine, and sulphapyridine, especially the former three, are of generalized use for topical therapy in ophthalmology. The fact that sulphanilamide is soluble in water only up to 0·8 per cent and that the other sulphas are still less soluble explains why at first, when only aqueous collyria were tried, local sulphonamide therapy did not make headway. Insufflation of powdered and microcrystal sulphonamides, their local application in properly chosen ointments, the use of sodium derivates, which are more soluble, the previous use of substances which break the surface tension and thus propitiate a larger penetration of sulphonamides through the cornea, the use of iontophoresis and other methods have been tried subsequently with good results and large concentrations achieved when oral or parenteral administration is used. Moreover, this high concentration is reached in a very short time. The possibility of combining local treatment of immediate effect and general treatment of delayed but constant effect is advantageous. Association of fever therapy increases the penetration ratio of the drug. So does local inflammation.

Since sulphonamides have only bacteriostatic action, it is essential that the drug be applied frequently; repeated instillations, application of suitable ointments, and iontophoresis appear to be the choice methods.

Phenomena of general intolerance for the sulphonamides during their topical use have not been mentioned so far. Local intolerance revealed by lid dermatitis and conjunctivitis have been mentioned; it always subsides as soon as the treatment is discontinued.

Therapeutic indication for sulphonamides locally in virus diseases is: in cases of inclusion conjunctivitis and trachoma. In the latter combined simultaneous massage and iontophoresis of the palpebral conjunctiva with the electrode, thus effecting drug penetration and at the same time destruction of the folliculi mechanically, have given good results.

In gonococcic conjunctivitis good results have been reported from the local use especially of sulphadiazine and sodium sulphacetamide. The seriousness of the disease, however, justifies combined local and oral treatment. In cases of streptococcus, pneumococcus, and Koch-Week's inflammations of the eye, sulphonamides are effective but have not proved themselves better than the other therapeutic agents, except in cases of corneal involvement, where iontophoresis is paramount. But in blepharitis, conjunctivitis, and corneal involvement due to staphylococcus, the topical use of sulphonamides is far superior to any other treatment. Thus in conjunctivitis, in general, the local use of sulphonamides is justified as a routine treatment. Ocular inflammation due to B. pyocyaneus has been treated with success with local applications of sulphonamides, especially with iontophoresis of sulphadiazine, Inflammations due to B. coli, B. proteus, and K. Friedlanderi have also responded favourably to local sulphonamide therapy.

Prophylactically, before and after ocular operations, the use of collyria of highly soluble sodium sulphacetamide has been advantageous.

Innocuous injections of sulphonamide solutions into the anterior chamber and into the vitreous chamber have been reported apparently with good clinical results.

Local sulphonamide therapy is very effective in a number of well-defined eye diseases, provided proper dosage and adequate means of administration are used.

Preservation of Stored Blood

The impact of war has led to considerable improvements in blood preservation, so that today efficient transfusion can

be carried out with blood that is two, three, or even four weeks old, and with the probability that the majority of cells will survive for a month or more after transfusion. Except therefore in some acute infections and certain hæmolytic anæmias there is no justification for the superstition that there is some special virtue in "blood on the hoof."

The investigations of many workers seem to justify the conclusion that the only way of assessing the value of a preservation is to measure the survival of the preserved cells after transfusion. It is true that bloods showing much lysis during storage do not survive well in a recipient's circulation; but the reverse is not true, for of two preservatives both giving equally good survival *in vitro*, one may be associated with unusually good cell preservation after transfusion while with the other survival may be quite poor. Acid-citrate solutions exemplify the first and dextrin citrate the second. The failure of *in vitro* tests is still not generally realised, and investigators, particularly abroad, often introduce new preservatives solely on the basis of their merits *in vitro*. Other accepted conclusions are that glucose aids cell survival *in vitro* and *in vivo*, and so does a small degree of acidity in the storage system. All this is confirmed and extended by Loutit (*J. Path. Bact.*, **57**:325, 1945) who finds that the optimum pH for storage is slightly less than that of the blood—between 7·1 and 7·3. Outside these limits, preservation *in vitro* and survival *in vivo* are deficient. Loutit also finds that the addition of diluent to 6% of the total volume enhances preservation; higher proportions make little difference. So too with citrate; apart from its essential anticoagulant action, a minimum amount is needed for good blood-preservation, but an increase above this level does not further assist cell survival. Loutit confirms that glucose is the most effective of the carbohydrate preservatives, while other sugars with very similar physical and chemical properties are much less satisfactory. He concludes that preservatives act whether by increasing the adhesion of molecules in the cell surface or by helping to maintain specific enzyme cycles within the cell.

Among some of the characteristics of the human erythrocyte are its high content of potassium, which in the circulation is paradoxically distributed in relation to the low potassium and high sodium of the plasma; another is the high content of phosphoric esters in the red cell and the low level of inorganic phosphate. According to Maizels (*Quart. J. Exper. Physiol.*, **32**:143, 1943-44), during the storage of blood phosphoric esters and cell potassium fall while inorganic phosphate and sodium rise, yet there is no correlation between the efficiency of a preservative and its ability to check these intracellular chemical degradations. It is clear that technical advances in blood preservation have far outstripped our knowledge of the way in which these agents act, and that even in the case of the apparently simple non-nucleated mammalian erythrocyte our knowledge of intracellular chemistry is still very incomplete. It may be that intensive study of enzyme systems within the erythrocyte will extend our knowledge of this subject and lead to still more efficient methods of blood preservation. At the moment it may seem sufficient that blood can be stored adequately for two or three weeks, but while atomic warfare and a resultant aplastic anæmia is a possible if remote contingency the need for research in longterm storage remains.—*Lancet*, **2**:605, 1945.

Medico-Legal Applications of Blood Grouping

The discovery of the ABO system of blood groups was soon utilized in connection with paternity cases and also for the typing of blood-stains. But the chance of exclusion of a wrongful accusation of paternity was not very great. Even with the subdivision of A into its two common subtypes the falsely accused man has, on the average, only one chance in six that he will be excluded by the determination of the blood group. Bloods or blood-stains are divisible into six kinds only—O, A_1, A_2, B, A_1B, A_2B. The establishment of the MN system constituted a notable medicolegal advance. In paternity cases it is of about equal value to the ABO system, so that the wrongfully accused man's chances improved to 1 in 3. There are three kinds of MN blood—M, N, and MN. Combining this threefold division with the sixfold division of the ABO system, human blood could now be divided into 18 types. A new blood group, Pl, established by Landsteiner and Levine (*J. Immunol*, **20**:179, 1931) and more recently reported on by Wiener and Sonn (*J. Lab. Clin. Med.*, **30**:395, 1945) seems to be clear-cut enough in its inheritance, P+ being dominant to P—. Its value in paternity cases, however, is negligible, for it would exclude only one wrongly accused person in every 100. For subdividing bloods, on the other hands, it is useful; with its help the 18 kinds of blood are increased to 36.

In the short-lived days of its pristine simplicity, when Rh + and Rh — alone were distinguished, the medico-legal contribution of the Rh system was no greater than that of P. All that is now greatly changed. If Fisher's (*Nature*, **153**:771, 1945) hypothesis of triple allelomorphs is established, as seems likely, there will exist no fewer than 27 serologically distinguishable kinds of Rh, though some of them are rare. Wiener and Sonn in the paper quoted above discuss the medico-legal implications of Rh, confining themselves to the eight Rh types upon which there has been general agreement for some time. They point out that the chances of the wrongfully accused man have now improved to nearly 1 in 2, while the distinguishable kinds of blood are 36×8=288. In this last connection, however, it must be pointed out that there is a serious limitation; Rh reactions are delicate and are applicable only to fresh, wet blood-stains.

The Rh system will make a further contribution, and there is every likelihood that new blood-group systems will be established in the near future. Callender, Race, and Paykoc (*Brit. M. J.*, **2**:83, 1945) described no fewer than three new antibodies, demonstrated during the course of repeated transfusions to an apparently hypersensitive patient. One of these is a Mendelian dominant, displayed by 8 to 9% of the English population. Truly, serology is making rapid strides towards justifying the opinion of Lansteiner that some day blood groups would be known to be as individual as finger-prints—*Brit. M. J.*, **2**:360, 1945.

Spontaneous Abortion

Hudson and Rucker (*J.A.M.A.*, **129**:542, 1945) write that ninety-four spontaneous abortions and 68 threatened abortions occurring in 1,000 consecutive pregnancies were studied. Treatment with bed rest and progesterone was followed by recovery in 43 per cent. However, 3 patients who were treated successfully had deformed babies (1 microcephalus and 2 spina bifidas). Falls and intercurrent infection were of no etiologic consequences in this series. Pelvic inflammatory disease was encountered only 3 times, but 2 of these patients aborted. One of the 4 patients with uterine fibroids aborted. Two of 8 diabetic patients aborted spontaneously. Overweight patients and those with low basal metabolic rates seem to be rather prone to abort. The same is true of patients who give the history of sterility. Forty-four and one-tenth per cent of the patients

who aborted had retrodisplacement of the uterus on postpartum examination as compared with 26·9 per cent of those who had term deliveries.

Pathogenesis and Diagnosis of Genital Tuberculosis

Arana (*Toko-Ginecl. Practice*, **3**:43, 1944, Ref. *Am. J. Obst. & Gynec.*, **50**:461, 1945) discusses tuberculosis localized in the tubes and the uterus.

The tubes may be infected by the circulatory and lymphatic routes and by contiguity. In recent and superficial infection, the tube is reddened, the fimbriæ are infiltrated; but the most typical lesion is found in the serosa in the form of small tubercles. The chronic process assumes the form of hydrosalpinx or pysalpinx, often bilateral and mobile because of lack of adhesions. The symptoms vary.

The uterus is one of the most frequent sites of tuberculosis of the genital apparatus, being involved in 50 per cent of the cases. The disease is secondary.

Lesions of the cervix are rare and may present the aspect of endocervicitis or of tuberculous ulcer of its vaginal portion. The posterior aspect of the cervix is more often involved than the anterior.

In general, uterine tuberculosis may occur at any age but it is more common during the period of genital activity, Symptoms vary; besides small hæmorrhages and general symptoms secondary to salpingitis and peritonitis which nearly always coexist, there is sterility, 5 per cent of which is due to uterine tuberculosis.

To discover genital tuberculosis, except in case of external lesions, it is necessary to think of it, because symptoms which permit making the diagnosis are rarely encountered. Because early tuberculosis of the genitalia is secondary, careful questioning nearly always discloses the primary focus. In clear-cut cases of active primary lesion, the presence of exudate in the peritoneal cavity, bilateral pelvic masses with little pain and with exacerbations, evening temperature, relatively low leucocytosis and sedimentation rate which does not correspond to the process found should arouse suspicion of tuberculous etiology of the tubal process, especially when these symptoms occur in a virgin.

The best method to establish the diagnosis of uterine tuberculosis is from the material obtained by curettage, part being reserved for histologic examination and part for animal inoculation. Prognosis is serious as to function but benign as to life. The only active treatment is ultraviolet irradiation which gives satisfactory results. Hygiene and diet must receive consideration. Roentgen rays in small doses may be used in inoperable cases and in those rebellious to physiotherapeutic treatment.

Synthetic Oestrogens in Malignant Disease

Dodds (*West London M. J.*, Ref. *J.A.M.A.*, **129**:567, 1945) who discovered the synthetic estrogen diethylstibestrol, has reviewed the present status of synthetic œstrogens in malignant disease. The fact that the female sex hormone responsible for secondary sexual characteristics can exist in three forms—œstrone, œstriol and œstradiol—suggested to him the possibility of producing œstrogens synthetically. These could be given by mouth. The first evidence that œstrogens might influence the course of malignant disease was produced by Kaufmann in 1935, when he showed the beneficial effect of natural œstrogens on kraurosis vulvae. This effect on a precancerous condition is perhaps the first indication of the value of these œstrogens in malignant disease. But it is in carcinoma of the prostate that the greatest interest in these substances has recently been shown. Nearly fifty years ago castration for the relief of symptoms of carcinoma of the prostate was widely advocated. In many cases the primary growth and the metastases decreased. The operation naturally was objectionable, and interest in the subject died down until revived by the work of the American surgeon Charles Huggins. The British genitourinary surgeon E. W. Riches stated at a joint meeting of the Pathological Society and the Biochemical Society that in his experience almost 95 per cent of the cases of carcinoma of the prostate respond to œstrogens.

Professor Dodds considers that the mode of action of œstrogens is obscure. The action may be on the pituitary by inhibiting the secretion of the gonadotropic hormone of the anterior lobe, it may be on the testes by suppressing the secretion of testosterone or it may be directly on the malignant growth itself. Of these hypotheses Dodds finds the first most attractive to the experimental biologist, but it is claimed that the effect of synthetic œstrogen is superior to castration. This would indicate that suppression of the function of the anterior lobe of the pituitary is not the sole explanation. While the relief of symptom occurs, cure cannot be claimed. But it must be remembered that diethyl-stilbœstrol is the first substance ever produced that has an action of any sort on cancer when administered by mouth. The success in carcinoma of the prostate has led to the use of œstrogens in every variety of carcinoma. In carcinoma of the breast beneficial effects have been obtained in only a small percentage of cases. Those recorded varied from slight relief to complete disappearance of the tumor and metastases. It is not known what type of case will respond or whether the effect is permanent.

Dermatologic Aspects of Poliomyelitis

Reys (*New York State J. M.*, **45**:1673, 1945) during the recent poliomyelitis epidemic in New York City, observed 84 children, their ages varying from infancy to 15 years, admitted to St. Francis Hospital with the diagnosis of poliomyelitis. The disease was more common in boys than in girls the ratio being 5 to 1. In 98 per cent of the children lesions were located on both infrapatellar areas, on the anterior and lateral aspects of both ankle joints, on the dorsa of both feet, on both soles and on the malleoli. These lesions were symmetrical and were typically those of hyperkeratinization in the form of plaques, small papules or slightly verrucous elevations, with roughness and dryness of the skin of the legs. Lesions of these types and forms are encountered in cases of vitamin A deficiency. Their abundance seemed to be proportional to the severity of the poliomyelitic involvement, their prominence disappearing with the abatement of the disease. Among the children who were admitted for other lesions, only 1 in 8 had such skin manifestations. From the extremely high incidence of these skin lesions in poliomyelitis, Reyes deduces that vitamin A deficiency may be a predisposing factor of poliomyelitis. He advises that a diet rich in vitamin A should be given to all children, especially during the periods of epidemics, and this diet should be supplemented by cod liver oil or its concentrates. Since vitamin A deficiency will produce keratinization of the epithelium of the skin and the mucous membranes of the internal systems, it is possible that these structures which have been affected by the keratinizing metaplasia are open doors for the

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NOTES & NEWS

LEPROSY CONTROL IN INDIA

The largest number of leprosy cases in the British Dominions is met with in India on account of the immense population, though the rate per 1,000 is much higher in Africa in such Colonies as Nigeria. In 1941 the Central Advisory Board of Health of the Government of India issued a report on leprosy and its control in India. This dealth with the efforts of the two previous decades to apply recent advances in our knowledge of treatment and of incidence and epidemiology, furnished by the surveys of E. Muir and I Santra, in controlling the disease by treating early cases on a large scale in numerous leprosy clinics, and in isolating the most infectious cases in leprosaria to keep down the number of new infections arising each year. The committee pointed out that dispensary out-patient treatment alone would not solve the problem and that little progress had recently been made in supplying the more expensive agricultural colonies for infective cases. The total number of leprosy cases in India is now estimated at 1,200,000 but fortunately only about one-tenth of them are highly infectious ones in urgent need of isolation. Only about 14,000 cases, including many uninfective nerve ones, are now isolated in India, but much remains to be done in this connexion before leprosy infections can be controlled and a start made in reducing the incidence of the disease. A paper by R. G. Cochrane (*Indian M. Gaz.* **79**:438, 1944) on leprosy control, with special reference to the Madras Presidency, is, therefore, timely. The essential is the appointment to each Province of an experienced leprologist, with status and emoluments that will attract suitable men. Where this has not already been done surveys are needed to ascertain the usually limited areas in which the high incidence of the disease constitutes it an important problem. In each of these a large agricultural colony should be established for the isolation and efficient treatment of as many as possible of the infective patients, who alone should be admitted to them. Seven such areas have been defined in the Madras Presidency, so the cost will be high, and it is lack of funds that has hitherto prevented this essential step being taken. The Lady Willingdon Leprosy Sanatorium should be developed as a centre for the Madras campaign, with provision for postgraduate teaching and research. In rural areas the isolation of infective cases at night in special house should be arranged for each infected village, because there are very few Indians who are well enough off to have the necessary accommodation to supply adequate home isolation. The care of uninfective, crippled nerve cases, who constitute most of the beggar class, is a philanthropic rather than a public health matter; they should be looked after in separate institutions or in distinct sections of colonies. The Mission to Lepers provides for many of them with the help of Government maintenance grants. In the Madras Presidency orders have been issued to ensure that lepers requiring in-patient or out-patient treatment are to be cared for at all Government hospitals and dispensaries. Children's sanatoria are also required. Wherever well-equipped agricultural colonies are provided there is no difficulty in filling them with suitable voluntary admissions, but instances occur in which highly infectious patients refuse such accommodation. The Madras Government is therefore amending the law to provide for the compulsory isolation of these few refractory patients. Funds should be forthcoming in support of a determined effort to solve the leprosy problem by putting into effect the comprehensive measures above outlined—*Brit. M. J.*

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entrance of the poliomyelitis virus into the human body. It should be investigated whether the administration of vitamin A either by mouth or parenterally, is of value in the treatment of poliomyelitis.

STATUS THYMOLYMPHATICUS

CARR (*J. Pediat,* **27**:1, 1945) writes that in the past six years, there were seen at San Francisco coroner's office 520 cases of sudden death in children below 10 years of age. Among these were 105 children who died apparently of suffocation. Among these there were 49 cases in which death was associated with pathologic changes in the thymus and the lymphatic system. This group offers examples of death from asphyxia following tracheal compression from an enlarged thymus gland, deaths from a partial obstruction by an enlarged thymus during or following anæsthesia, cases showing a combination of thymic enlargement, lymphatism and anaphylaxis, and cases of adrenal insufficiency associated with thymus hyperplasia. The widespread belief that an enlarged thymus in itself will not cause asphyxia by tracheal and auricular compression and distortion can be disproved at necropsy whenever studies are done on cases of sudden death in children. However, when once accepted, status thymolymphaticus and related terms become far too easy to use. Instead of being reserved for specific cases to which they properly apply, such diagnoses are generically used to explain many sudden deaths in children when there is no other obvious cause. Such diagnostic abuses have in the main been responsible for the disrepute of the thymic status. Orderly necropsy proceedings will reestablish the relationship of enlarged thymus glands, lymphatism, adrenal hypoplasia and such conditions, either isolated or related as true causes of death,

HEALTH EDUCATION AND VENEREAL DISEASE

The Army's experience with 8,000,000 men has provided an unusual opportunity to evaluate the effect of health education on the prevention of venereal disease. According to Larimore and Sternberg (*Am. J. Pub. Health,* **35**:799, 1945) the Army venereal disease educational program has applied virtually all of the accepted technics of health education. During 1944 the amount of graphic educational material distributed among the troops amounted to 15,000,000 pieces, and film audiences totalled 10,000,000. The program of instruction followed two lines: (1) to impart technical knowledge about venereal disease and (2) to motivate the individual to utilize this information at the time needed for the avoidance of venereal disease. Certain principles have been found essential for the successful use of education. Chief among these are (*a*) an integrated program, (*b*) the highest possible quality and attractiveness of all educational materials, (*c*) abandonment of the pedagogic concept of health education and substitution of a new approach of "health advertising," (*d*) avoidance of overemphasis of sex and (*e*) technical accuracy of all materials. It was easier to impart technical knowledge than to motivate the individual to utilize it. The following factors in motivation have been employed and have been found to be effective: fear, intelligence, pride, patriotism. Among the reasons for failure of motivation were (*a*) the nature of the sex urge itself, (*b*) "education for venereal disease" afforded by sexy motion pictures, comic strips, pin-up girls and the use of sex in certain advertising,

(*c*) "War psychology," (*d*) displacement of normal family and social relationships, (*e*) newer methods of treatment. (*f*) alcohol and (*g*) the state of morale. The strictly moral approach to the problem of avoiding venereal disease has been relatively ineffective in the Army. In measuring the results of the program, the authors state that the best single criterion is the extent of utilization of prophylaxis, which at the present time is at the rate of more than fifty million individual prophylactic items per month.—*J.A.M.A.*

SCIENCE IN THE U. S. S. R.

The war made impossible the free flow of publications as well as personal visiting between our country and the Soviet Union. In a recent article Prof. Arnold Sorsby regrets this the more because we have been so inadequately informed of Russian progress in medicine and science. During his visit there, early this year, with a group of scientists, he was impressed by the "assured place research has in the organisation of society." Distances are so great in that vast territory that the medical services as a whole, and research in particular, are decentralised. The medical services are indeed, conceived on a central plan, but each of the republics in the Union controls its own services, which supplement those of the Union as a whole. In addition, cities, industries, collective farms, and other labour organisations have their own services, supplementing the others. He sees Soviet medicine as a national medical service in its widest sense rather than as the State medical service.

Research is organised in the same liberal way. Some institutes are controlled by the USSR commissariat of health, others by the Academy of Medicine, or the governments of the various republics. The medical schools and universities take a large share in research. Different research departments work well together in spite of great sepecialisation. Thus in Moscow the institutes dealing with neurology, neurosurgery, occupational diseases, and ophthalmology all take the form of large clinical units with well-equipped clinical and research laboratories. They are staffed partly by whole-time laboratory workers, partly by others who have both clinical and laboratory duties. These different workers approach an agreed problem, each from his special angle, and this plan ensures that the laboratory workers are clear about the clinical needs, and the clinicians are aware of the possibilities and limitations of the laboratory. All clinical institutes are broadly planned with many special departments; so that work on ophthalmology, for example, is proceeding in the institutes of neurology, neurosurgery, and occupational therapy as well as in the institute of ophthalmology. The interlocking of research enables workers in the Soviet laboratories to learn more of unpublished work than is customary elsewhere, so that publication has not the same importance as in Great Britain. Professor Sorsby feels that this is one more reason for regretting our lack of personal contact with Soviet scientists.

The training of doctors has been adapted to needs over the past years: when a large increase was wanted, standards were not too exacting. In 1913 there were fewer than 20,000 doctors in the Czarist Empire; under the Soviet Union today there are 150,000 still too few. As numbers rose the standard of training was improved and its duration is now flaxed at six years in Moscow; training of this length is to be made universal within the next four years. Specialisation in the last year of training is no longer necessary. The Union, however, is continuing to train "feldschers," who are something like our old barber-surgeons. They undertake routine work under supervision. The persistence of this grade, Professor Sorsby suggests, is the prices paid for the intensive training of physicians; it will disappear in time. Students are paid during training, and their salary is raised each year. On qualifying they are required to do three years' service wherever in the USSR the need is greatest. Postgraduate study is the rule.

Prof. E. D. Adrian, FRS, who was also among those visiting the Soviet Union, notes that there have been few outstanding advances in physiology in recent years either in the USSR or elsewhere; but a general raising of Russian standards in training and equipment has shown its effects in the quality of the work published. The senior physiologists are of high repute, many of them pupils of Pavlov; and they are training juniors of like calibre. The central nervous system is keenly studied and new fields are being approached with new techniques. The output to be expected of this great body of physiologists, in years to come, will presumably exceed that of any country in Europe.—*Lancet.*

RHEUMATIC FEVER AND HEART DISEASE

The anuual Harveian Oration founded by William Harvey in 1656 was delivered on Oct. 19 at the Royal College of Physicians of London by Dr. John Parkinson, physician to the cardiac department of the London Hospital and to the National Heart Hospital.

Dr. Parkinson said that Harvey, by his discovery of the circulation, confined to the blood and the blood vessels the evil humours of early writers which were regarded as the cause of rheumatism. In the 17th century rheumatism was differentiated from gout; in the 18th century rheumatism was first recognized as being associated with the heart, and in the 19th century this association was confirmed.

Rheumatic fever of childhood was the main source of heart disease up to the age of 40. The damage was done between the ages of 5 and 15, and it exceeded tuberculosis as a cause of death to the age of 20. During this war, as in the last, large numbers of our young men were found unfitted for service because of valvular disease of the heart directly due to juvenile rheumatism. It was estimated that almost one-tenth of all rejections were on account of heart disease. In peace-time the economic loss each year could be judged by the fact that the duration of economic activity in these men was no more than ten years on the average. All were agreed that poverty and overcrowding were basic causes, and rheumatic fever was rare among children of the well-to-do. Anything a Government did in these directions would reduce the incidence of rheumatic heart disease.

Dr. Parkinson said there was almost unanimous opinion that compulsory notification of rheumatic fever was essential to progress, for it would permit its early diagnosis before heart disease had taken hold. The excellent scheme for rheumatic children now in operation by the London County Council was regarded in the United States and elsewhere as the most comprehensive in existence; but doctors knew, and the public should know, that institutional treatment from the outset, and subsequent supervision, would have to be extended to every case of rheumatic fever occurring in this country. There should now be created a Rheumatic Fever Committee to

co-ordinate research and plan for the future. The Orator believed that the Royal College of Physicians was prepared to take a lead in this great endeavour. The objective should include one main county hospital for research, and hospitals and clinics to serve all densely populated areas. Ultimately it would be found necessary as it had been in the United States, to create a National Council for Rheumatic Fever and Heart Disease—*Brit. M. J.*

MEDICAL POETS

Many medical men in this country have been poets—one bibliography gives 156 names—but only two, in the view of Sir Arther MacNalty, who devoted his presidential address in the History Section of the Royal Society of Medicine to the influence of medical poets on English poetry, have scaled the heights of Parnassus. Those two were John Keats and Robert Bridges, and both of them abandoned medicine for poetry.

Sir Arthur MacNalty traced medical poets from the Spenserian period, beginning with Phineas Fletcher (1582-1650). The most noteworthy name among Elizabethan poet-physicians was Thomas Campion (1567-1619), who was educated at Peterhouse, Cambridge, but took no degree. His first collection of poems appeared in 1601, but not until 1606 did his name appear as a doctor of physick; he had probably studied medicine at one of the Continental universities. W. E. Henley described him as a curious metricist, and Sir Sylvanus Vivian, who edited his work, said that he was a master of subtle cadences. Sir Thomas Browne (1605-82) was not often thought of as a poet, but the *Religio Medici* was one of the most beautiful prose poems in the language, belonging to that briliant age before poetry and prose divided their domain. A medical poet of the time of James I was Abraham Cowley (1618-67), an exponent of the metaphysical flight in poetry, whose lyrics survived in modern anthologies. Cowley never practised medicine, but, believing botany necessary to a physician, composed several books on herbs, flowers, and trees. Another medical poet of this period was Henry Vaughan (1621-95). In the neo-Augustan period there were many medical poets and wits, among them John Arbuthnot (1667-1735), friend of Pope and Swift, Sir Samuel Garth (1661-1719), Sir Richard Blackmore (1650-1729), and, in spirit if not strictly in time, Mark Akenside (1721-70), who had true poetic gifts, though his first works were overrun by learning and exactitude. Erasmus Darwin (1731-1802) must be mentioned if only for his poem *Botanic Garden*, Goldsmith (1728-74) as representing the new age in poetry when it began to deal with nature and everyday life, and Crabbe (1754-1832) as one of the last of the classicists in form and one of the first of the realists in matter.

Then came Keats (1795-1821), whose writing was the reincarnation of the Greek spirit of poetry, and whose far reaching influence was traceable among the poets of the Victorian age. Lovell Beddoes (1803-49) had never received due recognition, perhaps because he never decided whether to devote himself exclusively to physiology or to dramatic poetry. Medicine's poet laureate was Robert Bridges (1844-1930)—her only laureate, though Southey was for a short time a medical student in the department of anatomy at Oxford. Bridges's *Testament of Beauty*, published in 1929 on his 85th birthday, was unique as the work of an octogenarian. Of his earlier poems, *On a Dead Child* could probably only have been written by one who had been a children's physician. The name of Ronald Ross should be mentioned; and Henry Head and Charles Sherrington

(*Continued at foot of next column*)

CORRESPONDENCE

The Editor is not responsible for any views expressed by contributors

IDIOPATHIC PULMO-EOSINOPHILAEMIA

SIR,—I have just come across the article of Dr. S. S. Misra in the November, 1945 number of the J.I.M.A. and in the interests of accuracy I might say that the late Dr. C. Frimodt Moller and I did not label the symptom complex referred to as "pseudo-tuberculosis with eosinophilia". The title of the paper was "A Pseudo-tuberculous condition associated with Eosinophilia". We intentionally avoided 'Pseudo-tuberculosis' as being misleading, but, as in 1940 we had no name for the syndrome, we gave a descriptive title rather than a definitive name. Those who have investigated the syndrome since have apparently been in similar difficulties and it is unlikely that Dr. Misra's own suggestion "idiopathic pulmo-eosinophilæmia" will meet with general acceptance. Weingarten's "tropical eosinophilia" is also not likely to be the permanent name as it takes just one of the symptoms and as Dr. Misra suggests gives an artificial geographical narrowness which may not be correct. An acceptable name will probably be found when the aetiology of the disease is better understood.

Dr. Misra also writes "'pseudo-tuberculosis' is a very unfortunate choice because of the tragic association with

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(*Continued from previous column*)

had written poems of merit in intervals between their scientific work. But it was evident, Sir Arthur MacNalty concluded, that a divided allegiance prevented the attainment of the sublimest heights in poetry. It was fortunate that John Keats laid down his lancet to take up his lyre. The student of medicine who received the divine afflatus should decide forthwith at which altar he would serve if he desired to be pre-eminent in either calling—*Brit. M. J.*

DRUGS CONTROL ORDER, 1945

The following is a copy of letter No. 11 D.M.(2)/45 dated 11/14th January, 1946, from the Asstt. Secretary to the Government of India Department of Industries and Supplies to the Hony. General Secretary, Indian Medical Association, Calcutta:

"I am directed to refer to paragraph 6 of the minutes of the 8th meeting of the Drugs Control Advisory Committee held on the 3rd January, 1946, a copy of which has been forwarded to you with this Department letter No. 3 D.M.(12)/45 dated 10-1-46 and to say that the Government of India has agreed to exempt Registered Medical Practitioners from the necessity of taking out a Purchaser's permit under Clause 5 of the Drugs Control Order for purchasing controlled drugs from importers, manufacturers and wholesalers. A notification giving effect to the decision will be published shortly in the Gazette of India."

GREETINGS TO I.M.A. MEMBERS

Councillor Dr. D. R. Prem, Chairman of Birmingham India League (39, Welford Road, Sutton Coldfield), sends to the members of Indian Medical Association his best wishes for a merry Christmas and happy and peaceful New Year.

Dr. Prem adds, "May 1946 see India as a free and Independent Nation, playing her part in establishing lasting peace and freedom of mankind."

tuberculosis". Even if 'pseudo tuberculosis' had been the name employed 'tragic' is a wrong word to use, specially for a doctor. The disease in question, having many of the symptoms of tuberculosis, and often an x-ray picture which can be mistaken for tuberculosis was and is still continually being diagnosed as that disease; and even if it is treated as tuberculosis instead of with arsenic therapy which Dr. Misra admits is sometimes disappointing, the results are often clinically quite good. The mental attitude of 'tragic' as applied to tuberculosis should be a thing of the past. I am, etc.

Union Mission Tuberculosis Sanatorium

R. M. BARTON.

THREE QUESTIONS

SIR,—I would be grateful if you can publish 3 questions in your Journal and by the time get answers to them by lecturers of the faculty or experts.

I. What is the reason that most of the Indian doctors order in diabetics: *wheat* instead of *rice?* I found that some kinds of wheat contain sometimes even more starch than rice and would then prefer rice if carbohydrates cannot be avoided totally.

II. There is a skin disease, between 'Pityriasis' and 'Leucoderma'. In Tamil it is called 'Taemel'. It is scaling and leads to white patches all over the body. I never saw "pityriasis rosea" caused by microsporon furfur causing depigmentation in Europe. Please state aetiology, course, description and treatment and if the patches can become darker again. Leucoderma does not scale like 'Taemel' does. A dermatologist may write about it. Another item is just on the contrary matter: black hyperpigmentations under the eyes. What is the cause and treatment?

III. About artificial table-salt I would like to hear a pharmacologist. Sometimes should the sodium ion be avoided and the Rock-salt be used in nephritis, œdema. But I know that sodium formicicum (formate) was widely used, only I don't know the reason. The latter avoids the chlor ion. May be that in some kidney cases neither sodium alone, nor chlor alone but the combination of both together does harm? Which ion is to avoid in hypertony? (the sodium, chlor, or the combination of both?). There is the German-made 'Citrovin', an artificial table-salt, avoiding chlorine only, for nephritis, hypertony due kidney disease and essential hypertony, decompensated heart diseases, allergic diseases. This salt contains sodium, potassium, calcium, magnesium salts bound with organic acids. Why is the chlorine ion avoided?

Trichinopoly. DR. BEER.

A CASE OF SCORPION VOMIT*

SIR,—One Hindu male aged about 38 years old came to me at about 10 A.M. complaining of feverishness with vigor for the last 5 or 6 days. His temperature on the day was 99°F. No spleen could be palpated. He had suffered from malaria several times in the malaria season of 1943 and had always remained under my treatment. I diagnosed malaria this time and gave 3 doses of quinine mixture. He did not take any dose and at 12 noon he vomited with one scorpion on the plastered floor.

At once two children ran to me and said that their father had vomited one scorpion. I rushed to the place. The patient was nervous. I found the scorpion alive in the vomit. His wife was weeping. I assured them several times that the scorpion can not be with the vomit from the stomach and it might be already on the floor. But none of them would agree with me. His wife told me that she had seen with her own eyes the falling of scorpion on the floor with the vomit. The patient himself gave the same statement. His two sons about 10 and 12 years old also say the same thing. Vomiting was a bit excessive with blood. He also got fever with rigor and looked exhausted. His wife wept all the more when she saw blood in the vomit. She was sure that her husband could not remain alive as he had vomited a scorpion and there was blood mixed with the vomit.

I gave him one injection of Quinine bi-hydrochloride gr. X in 2 c.c. with saccharose solution and sent two powders of aspirin gr. V, sodi bicarb gr. XV, glucose gr. XV and two doses of digestive mixture. His wife came to me at 1-30 P.M. and told me that the condition was a little better. I advised them to give ice to suck, orange juice and cardamoms. I was not convinced that the scorpion came out with the vomit. The patient and his wife were not convinced about my opinion. So I request you to publish this case note with your remark.

Ghaziabad. BALWANT RAI AGARWAL, L.S.M.F.

* This unusual case is interesting, and is published with the idea of stimulating discussions.—ED., *J.I.M.A.*

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